

YOU HAVE REQUESTED DATA FROM 122 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:69153 CAPLUS Full-text

DN 140:246406

TI HnRNP L enhances sensitivity of the cells to KW-2189

AU Taguchi, Fumiko; Kusaba, Hitoshi; Asai, Akira; Iwamoto, Yasuo; Yano, Keiichi; Nakano, Hirofumi; Mizukami, Tamio; Saijo, Nagahiro; Kato, Harubumi; Nishio, Kazuto

CS Pharmacology Division, National Cancer Center Research Institute, Tokyo, Japan

SO International Journal of Cancer (2003), Volume Date 2004, 108(5), 679-685

CODEN: IJCNW; ISSN: 0020-7136

PB Wiley-Liss, Inc.

DT Journal

LA English

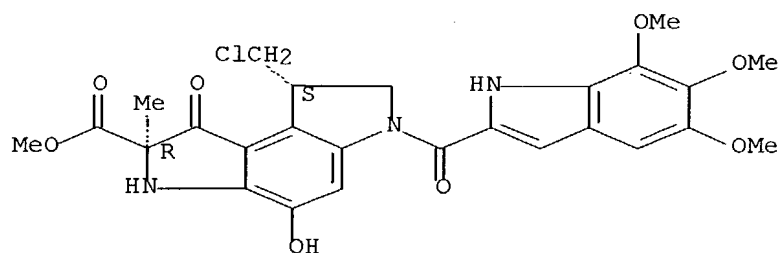
AB Heterogeneous nuclear ribonucleoproteins (hnRNPs) are involved in several RNA-related biol. processes. We demonstrated hnRNP L as a candidate protein of DARP (duocarmycin-DNA adduct recognizing protein) by gel shift assay and amino acid sequencing. Stable transfectants of hnRNP L showed high sensitivity of the cells to the growth inhibitory effect of KW-2189, a duocarmycin derivative in vitro. Immunostaining of hnRNP L demonstrated differential intracellular localization of hnRNP L among human lung cancer cell lines. A transfection study using a series of deletion mutants of hnRNP L fused to indicate that the N-terminal portions of RRM(RNA recognition motif)1, RRM3 and RRM2 are involved in localization of hnRNP L. We identified sequences in these portions that have high homol. with the sequences of known NLS (nuclear localization signal) and NES (nuclear export signal). HnRNP L is a factor that detes. the sensitivities of cancer cells to the minor groove binder, and overexpression and differential intracellular localization of hnRNP L are involved in its function in lung cancer.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:532329 CAPLUS Full-text
 DN 139:106453
 TI p-Amidobenzyl ethers of drugs in drug delivery systems
 IN Senter, Peter D.; Toki, Brian E.
 PA USA
 SO U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S. Ser. No. 963,103.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003130189	A1	20030710	US 2002-252947	20020923
	US 2003096743	A1	20030522	US 2001-963103	20010924
	WO 2003026577	A2	20030403	WO 2002-US30282	20020924
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2001-963103	A2	20010924		
	US 2002-252947	A	20020923		
OS	MARPAT 139:106453				
AB	Compns. containing conjugates containing a drug moiety, a ligand and an optional acyl unit, an amino acid or a peptide, an aminobenzyl ether self-immolative spacer group, an optional second self-immolative group, and carriers, diluents and/or excipients, and methods of delivery the drug are described. Thus, a peptide was treated with 1-naphthol to give a derivative The compound was very stable in human serum, and showed antitumor activity.				
IT	118292-36-7D , Duocarmycin C2, conjugates with minor groove binders 124325-94-6D , Duocarmycin B2, conjugates with minor groove binders RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amidobenzyl ethers of drugs in drug delivery systems)				
RN	118292-36-7 CAPLUS				
CN	Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)- 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H- indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)				

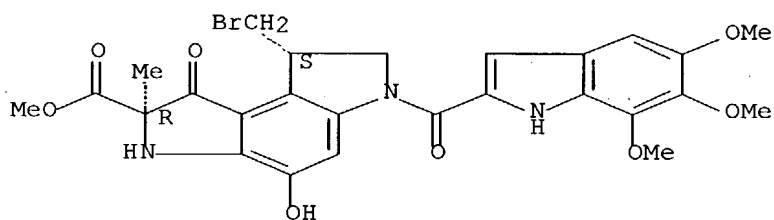
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 3 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:473962 CAPLUS Full-text

DN 139:145374

TI Rapid determination of sequence selectivity and stability of alkylated oligonucleotide adducts by electrospray tandem mass spectrometry

AU Colgrave, Michelle L.; Iannitti-Tito, Paula; Wickham, Geoffrey; Sheil, Margaret M.

CS Department of Chemistry, University of Wollongong, Wollongong, 2522, Australia

SO Australian Journal of Chemistry (2003), 56(5), 401-413
CODEN: AJCHAS; ISSN: 0004-9425

PB CSIRO Publishing

DT Journal

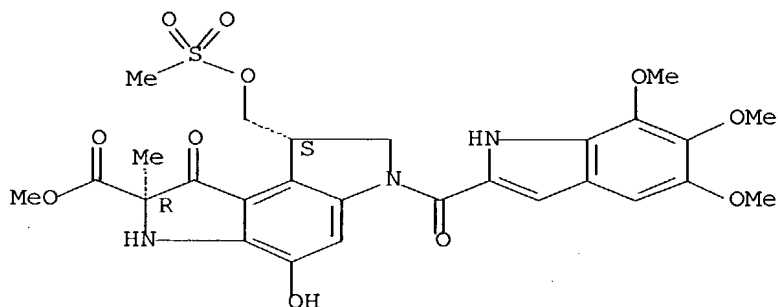
LA English

AB The binding of the antitumor antibiotics, duocarmycin C2 (pyrindamycin A), duocarmycin C1 (pyrindamycin B), hedamycin, and DC92-B to self complementary oligonucleotides (ranging from 6 to 14-mers) has been studied using electrospray ionization mass spectrometry (ESI-MS) and tandem mass spectrometry (MS/MS). The duocarmycins bind via non-covalent interactions in the minor groove of DNA with subsequent alkylation of the N3 atom of adenine. Hedamycin and DC92-B are intercalating, alkylating agents that target the N7 of guanines within 5'-CGT, and to a lesser extent, 5'-CGG sequences. We show here that the site(s) of alkylation by these ligands are strongly influenced by the location of high affinity binding sites within these short oligonucleotides. These data clearly demonstrate value of using ESI-MS/MS to pre-screen ligand-oligonucleotide complexes prior to performing more detailed structural studies, since subtle selectivity differences have been detected by this technique that were not evident from conventional sequencing studies on larger segments of DNA.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

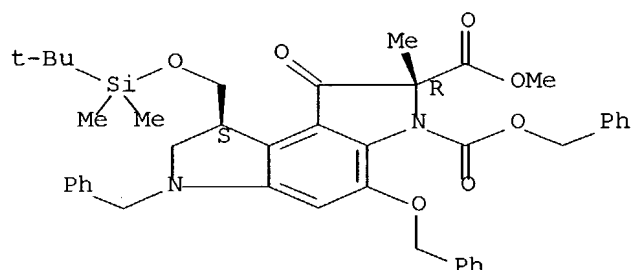
L10 ANSWER 4 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:361118 CAPLUS Full-text
 DN 139:85138
 TI Total Synthesis of the Duocarmycins
 AU Yamada, Ken; Kurokawa, Toshiki; Tokuyama, Hidetoshi; Fukuyama, Tooru
 CS Graduate School of Pharmaceutical Sciences, University of Tokyo, Bunkyo,
 Tokyo, 113-0033, Japan
 SO Journal of the American Chemical Society (2003), 125(22), 6630-6631
 CODEN: JACSAT; ISSN: 0002-7863
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 139:85138
 AB The total synthesis of (+)-duocarmycin A and SA through a common
 indoline intermediate is described. The key reactions include selective
 lithiation of a 2,6-dibromiodobenzene derivative and diastereoselective
 addition to a chiral nitroalkene, copper-mediated aryl amination, and
 addition of aryllithium to azlactones.
 IT 157478-24-5P 556038-50-7P 556038-51-8P
 556038-64-3P 556038-65-4P 556038-66-5P
 556038-67-6P
 RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic
 preparation); BIOL (Biological study); PREP (Preparation); RACT
 (Reactant
 or reagent)
 (preparation of (+)-duocarmycin A and SA from a common indoline via
 selective lithiation, copper-mediated aryl amination, and
 diastereoselective addition)
 RN 157478-24-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-
 hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 556038-50-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-2-
 methyl-1-oxo-4-(phenylmethoxy)-6-(phenylmethyl)-, 2-methyl
 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

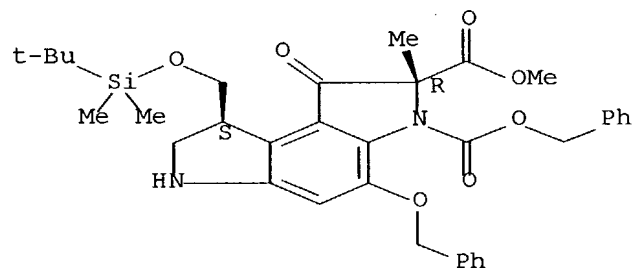
Absolute stereochemistry. Rotation (+).



RN 556038-51-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-2-
methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 3-(phenylmethyl) ester,
(2R,8S)-
(9CI) (CA INDEX NAME)

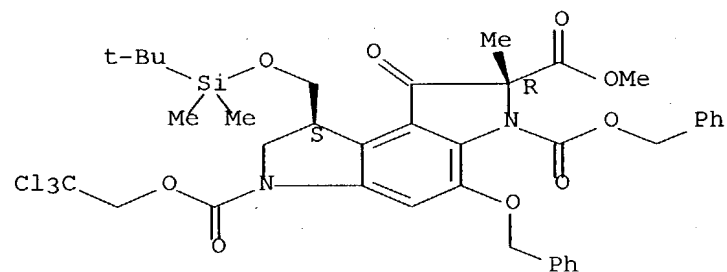
Absolute stereochemistry. Rotation (+).



RN 556038-64-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,2,7,8-tetrahydro-2-
methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 3-(phenylmethyl)
6-(2,2,2-trichloroethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

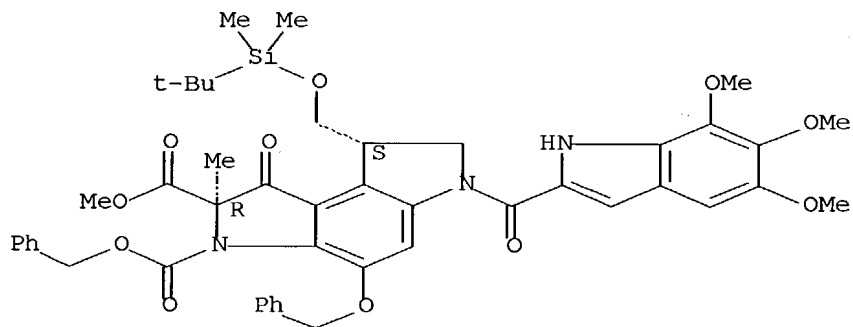


RN 556038-65-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-2-
methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-
yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA

INDEX
NAME)

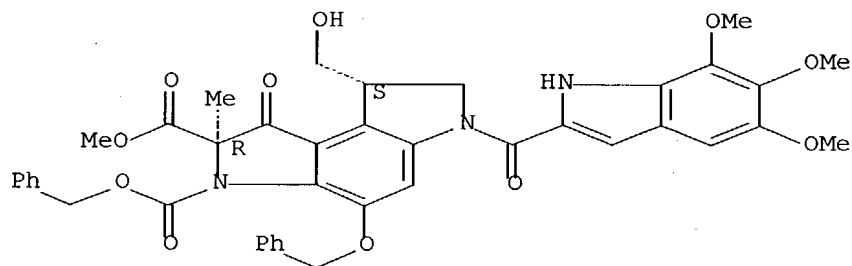
Absolute stereochemistry. Rotation (+).



RN 556038-66-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
1,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl)
ester, (2R,8S)- (9CI) (CA INDEX NAME)

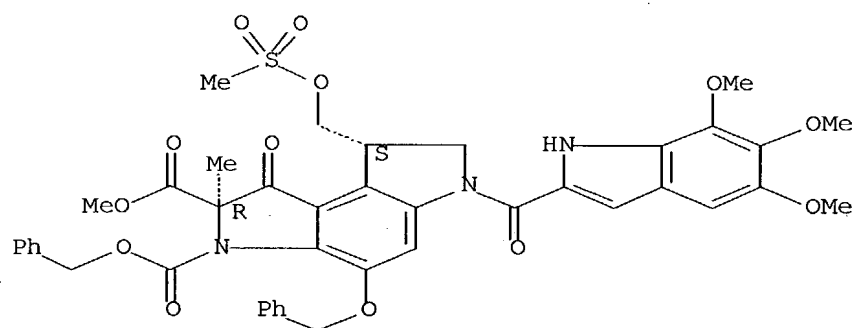
Absolute stereochemistry. Rotation (+).



RN 556038-67-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
1,6,7,8-tetrahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-
(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl
3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 556038-57-4P 556038-58-5P 556038-59-6P
556038-69-8P 556038-70-1P 556038-71-2P
556038-72-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation of (+)-duocarmycin A and SA from a common indoline via selective lithiation, copper-mediated aryl amination, and diastereoselective addition)

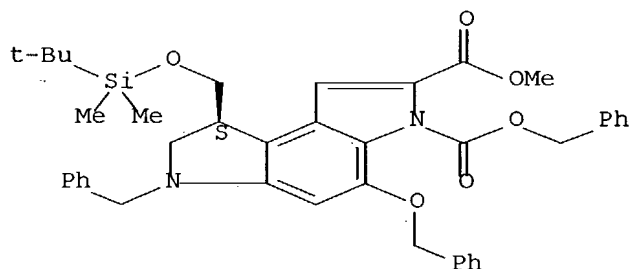
RN 556038-57-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-
(phenylmethoxy)-6-(phenylmethyl)-, 2-methyl 3-(phenylmethyl) ester,

(8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



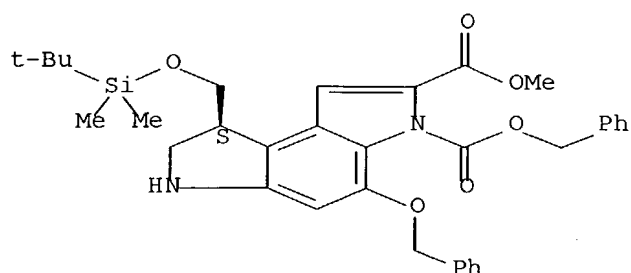
RN 556038-58-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-
(phenylmethoxy)-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA

INDEX

NAME)

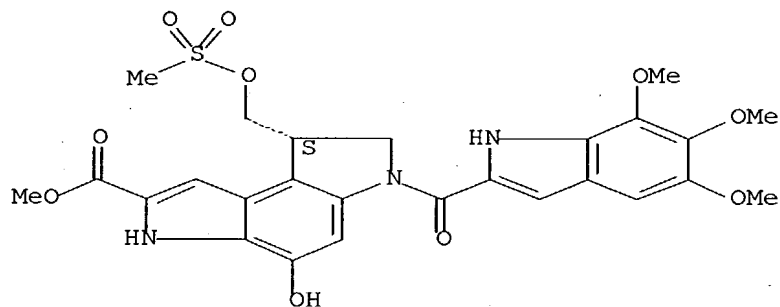
Absolute stereochemistry. Rotation (+).



RN 556038-59-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 3,6,7,8-tetrahydro-4-hydroxy-8-[[(methylsulfonyl)oxy]methyl]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

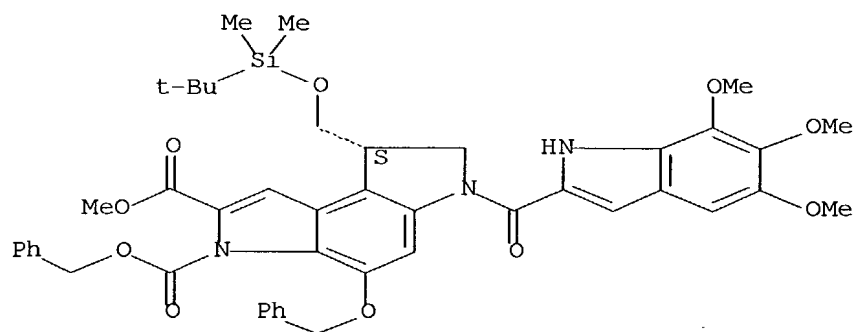
Absolute stereochemistry. Rotation (+).



RN 556038-69-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)

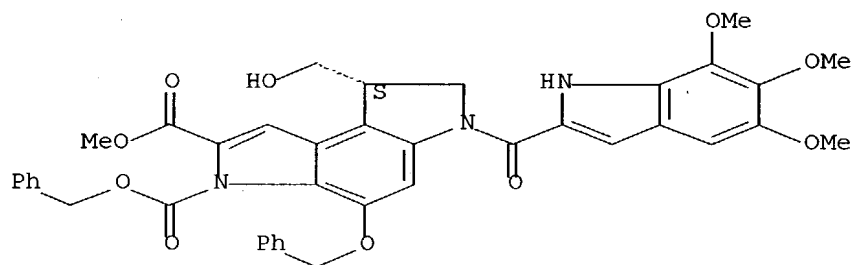
Absolute stereochemistry. Rotation (+).



RN 556038-70-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethoxy) ester, (8S)- (9CI) (CA
INDEX NAME)

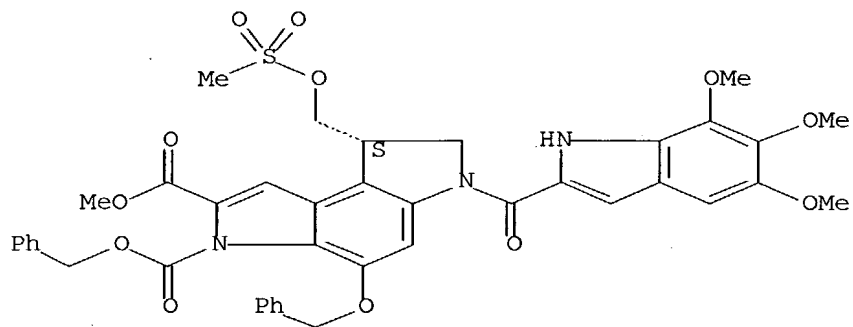
Absolute stereochemistry. Rotation (+).



RN 556038-71-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,
7,8-dihydro-8-[(methanesulfonyl)oxy]methyl]-4-(phenylmethoxy)-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethoxy) ester,
(8S)- (9CI) (CA INDEX NAME)

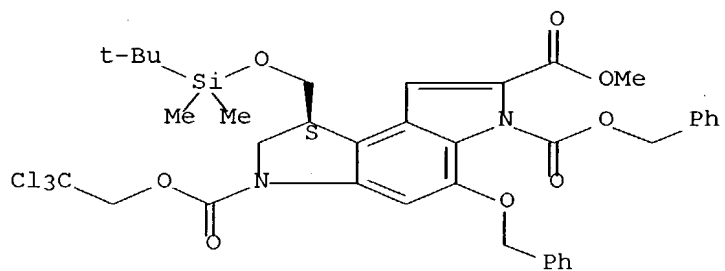
Absolute stereochemistry. Rotation (+).



RN 556038-72-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-
(phenylmethoxy)-, 2-methyl 3-(phenylmethyl) 6-(2,2,2-trichloroethyl)
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

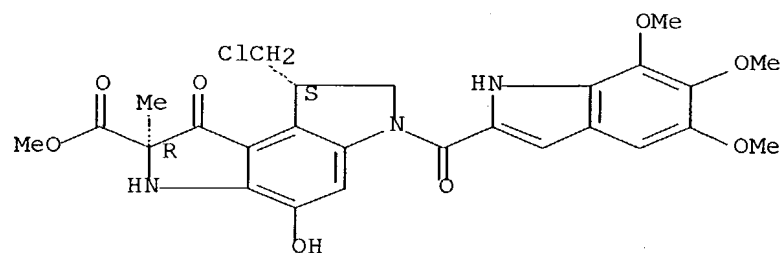


RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:261611 CAPLUS Full-text
 DN 138:292740
 TI p-Amidobenzyl ethers in drug delivery agents
 IN Senter, Peter D.; Toki, Brian E.
 PA Seattle Genetics, Inc., USA
 SO PCT Int. Appl., 109 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003026577	A2	20030403	WO 2002-US30282	20020924
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003096743	A1	20030522	US 2001-963103	20010924
	US 2003130189	A1	20030710	US 2002-252947	20020923
PRAI	US 2001-963103	A	20010924		
	US 2002-252947	A	20020923		
OS	MARPAT 138:292740				
AB	Comps. [L-[-An-Z-X-Ww-]-D and B-[-Z-X-Ww-]-D, where D is a drug moiety, L is a ligand, B is a blocking group, A = acyl Z = amino acid or a peptide, X = aminobenzyl ether spacer group, W = optional second group, n = 0 or 1, and w = 0 or 1] and compns. of the compds. with carriers, diluents and/or excipients, and methods of delivery of the drugs are disclosed. Thus, etoposide was allowed to react with a peptide-containing and the product obtained was shown to be very stable at pH 5.1 and 7.2 after 7 days.				
IT	118292-36-7D , Duocarmycin C2, conjugates with minor groove binders 124325-94-6D , Duocarmycin B2, conjugates with minor groove binders RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amidobenzyl ethers as drug delivery agents)				
RN	118292-36-7 CAPLUS				
CN	Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)				

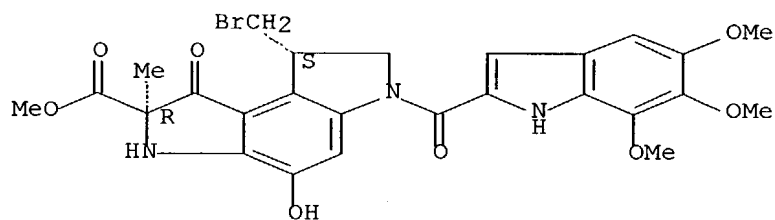
Absolute stereochemistry.



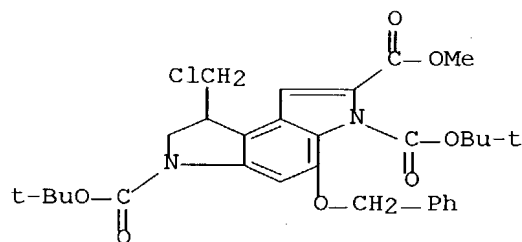
RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

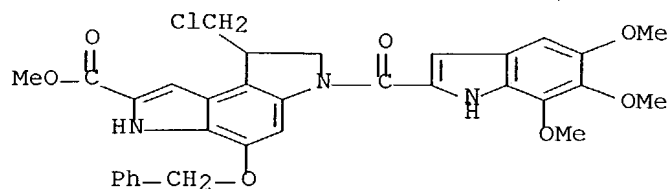
Absolute stereochemistry.



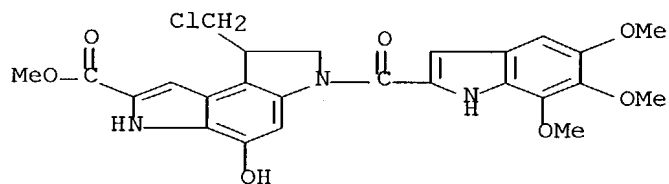
L10 ANSWER 6 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:109220 CAPLUS Full-text
 DN 139:22032
 TI A concise and efficient synthesis of seco-duocarmycin SA
 AU Tietze, Lutz F.; Haunert, Frank; Feuerstein, Tim; Herzig, Tobias
 CS Institut für Organische Chemie der Georg August Universität Göttingen,
 Göttingen, 37077, Germany
 SO European Journal of Organic Chemistry (2003), (3), 562-566
 CODEN: EJOCFK; ISSN: 1434-193X
 PB Wiley-VCH Verlag GmbH & Co. KGaA
 DT Journal
 LA English
 OS CASREACT 139:22032
 AB A short and efficient synthesis of seco-duocarmycin SA [8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid Me ester], a highly potent cytostatic agent and direct precursor of the natural product duocarmycin SA, has been achieved. Starting from com. available 2-methoxy-4-nitroaniline the synthetic protocol contains a Fischer indole synthesis to introduce the heterocyclic scaffold and a radical 5-exo-trig cyclization to furnish the (chloromethyl)indoline ring system as key reactions.
 IT **539856-46-7P 539856-47-8P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (concise and efficient synthesis of seco-duocarmycin SA)
 RN 539856-46-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 3,6-bis(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 539856-47-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



IT **144667-38-9P**, Seco-duocarmycin SA
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (concise and efficient synthesis of seco-duocarmycin SA)
 RN 144667-38-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl
 ester (9CI) (CA INDEX NAME)

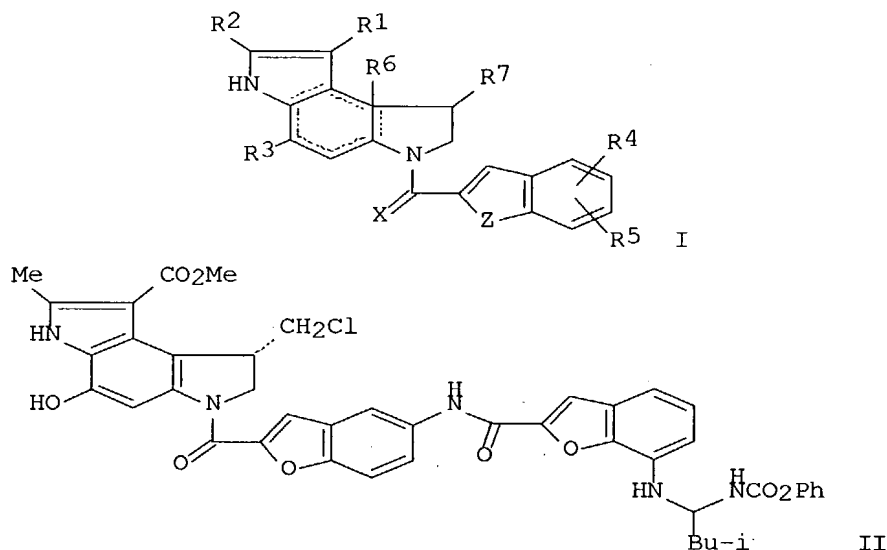


RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:954878 CAPLUS Full-text
DN 139:30289
TI Regulation of gene expression by sequence-specific alkylating polyamide
AU Oyoshi, Takanori; Kawakami, Wakana; Bando, Toshikazu; Narita, Akihiko;
Sugiyama, Hiroshi
CS Division of Biofunctional Molecules, Institute of Biomaterials and
Bioengineering, Tokyo Medical and Dental University, Tokyo, 101-0062,
Japan
SO Nucleic Acids Research Supplement (2002), 2 (Twenty-ninth Symposium on
Nucleic Acids Chemistry), 259-260
CODEN: NARSCE
PB Oxford University Press
DT Journal
LA English
AB In order to investigate the inhibition of gene expression by a new type
of hairpin polyamide-CPI conjugate 1, its ability to inhibit
transcription in cell free system was investigated. Sequence-selective
alkylation of double-stranded DNA by 1 was investigated by denaturing
gel electrophoresis using 1000 bp DNA fragment which codes for green
fluorescence protein (GFP) under the control of T7 promoter. Anal. of
DNA sequence indicated that 1 alkylated predominantly at the site of 5'-
AGTCA-3' in coding region of GFP. The transcript by T7 RNA polymerase
using the alkylated DNA as a template was analyzed by PAGE. The results
clearly indicate that 1 inhibits transcription by alkylation of coding
region at a nanomolar concentration
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:927432 CAPLUS Full-text
 DN 138:4470
 TI Preparation of duocarmycin analogs as potent cytotoxins
 IN Ng, Howard P.; McGee, Danny P. C.; Wu, Guoxian; Li, Zhihong; Gangwar, Sanjeev; Saunders, Oliver L.; Martichonok, Valeri; Astafieva, Irina; Moore, Jimmie; Yarranton, Geoffrey Thomas; King, David J.; Boyd, Sharon; Lobl, Thomas J.
 PA Coulter Pharmaceutical, Inc., A Wholly Owned Subsidiary of Corixa Corporation, USA
 SO PCT Int. Appl., 118 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002096910	A1	20021205	WO 2002-US17210	20020531
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003050331	A1	20030313	US 2002-160972	20020531
	US 2003064984	A1	20030403	US 2002-161234	20020531
	US 2003073852	A1	20030417	US 2002-161233	20020531
PRAI	US 2001-295196P	P	20010531		
	US 2001-295259P	P	20010531		
	US 2001-295342P	P	20010531		
	US 2001-304908P	P	20010711		
OS	MARPAT 138:4470				
GI					



AB Duocarmycin analogs I [X, Z = O, S, or imino; R1 = H, (un)substituted alkyl, carboxylic acid, ester, or amide; R2 = H, (un)substituted alkyl; R3 = :O, OH or derivative; R4, R5 = H, (un)substituted alkyl, (hetero)aryl, heterocycloalkyl, halo, NO₂, NR₁₅R₁₆, NCOR₁₅, O₂CNR₁₅R₁₆, OCO₂R₁₅, COR₅, OR₁₅, where R₁₅ and R₁₆ = H, (un)substituted (hetero)alkyl, (hetero)aryl, heterocycloalkyl, or peptidyl or NR₁₅R₁₆ = (un)substituted 4-6 membered heterocycloalkyl; R6 = a single bond; R7 = CH₂-X, where X is a leaving group; or R6 and R7 may form a cyclopropyl ring] were prepared as potent cytotoxins. Peptidyl and disulfide linkers are cleaved in vivo. The linkers are of use in forming prodrugs and conjugates of the cytotoxins of the invention as well as other diagnostic and therapeutic moieties. Thus, compound II was prepared via acylation of the 5-amino-2-benzoyl intermediate. Compds. I generally have an IC₅₀ value in a proliferation assay of .apprx. 1-100 nM, preferably .apprx. 10-10 nM.

IT 477207-70-8P 477207-71-9P 477207-72-0P
 477207-73-1P 477207-74-2P 477207-75-3P
 477207-76-4P 477207-77-5P 477207-78-6P
 477207-79-7P 477207-80-0P 477207-81-1P
 477207-82-2P 477207-83-3P 477207-84-4P
 477207-85-5P 477207-86-6P 477207-87-7P
 477207-92-4P 477207-95-7P 477207-96-8P
 477207-97-9P 477207-99-1P 477208-00-7P
 477208-02-9P 477208-04-1P 477208-05-2P
 477208-07-4P 477208-08-5P 477208-09-6P
 477208-10-9P 477208-11-0P 477208-12-1P
 477208-13-2P 477208-14-3P 477208-18-7P
 477208-21-2P 477208-22-3P 477208-23-4P
 477208-24-5P 477208-25-6P 477208-26-7P
 477208-27-8P 477208-28-9P 477208-32-5P
 477208-33-6P 477208-34-7P 477208-39-2P
 477208-40-5P 477208-41-6P 477208-42-7P
 477208-43-8P 477208-44-9P 477208-45-0P

477208-46-1P 477208-47-2P 477208-48-3P
477208-49-4P 477208-50-7P 477208-51-8P
477208-52-9P 477208-53-0P 477208-54-1P
477208-55-2P 477208-56-3P 477208-57-4P
477208-58-5P 477208-59-6P 477208-60-9P
477208-61-0P 477208-62-1P 477208-63-2P
477208-64-3P 477208-65-4P 477208-66-5P
477208-67-6P 477208-69-8P 477208-70-1P
477208-71-2P 477208-72-3P 477208-73-4P
477208-75-6P 477208-77-8P 477208-78-9P
477208-79-0P 477208-80-3P 477208-81-4P
477208-82-5P 477208-83-6P 477208-84-7P
477208-85-8P 477208-86-9P 477208-87-0P
477208-88-1P 477208-89-2P 477208-90-5P
477208-91-6P 477208-92-7P 477208-93-8P
477208-94-9P 477208-95-0P 477208-96-1P
477208-97-2P 477208-98-3P 477208-99-4P
477209-00-0P 477209-01-1P 477209-02-2P
477209-03-3P 477209-04-4P 477209-05-5P
477209-06-6P 477209-07-7P 477209-08-8P
477209-09-9P 477209-10-2P 477209-11-3P
477209-12-4P 477209-14-6P 477209-15-7P
477209-16-8P 477209-17-9P 477209-18-0P
477209-19-1P 477209-20-4P 477209-21-5P
477209-23-7P 477209-24-8P 477209-25-9P
477209-26-0P 477209-27-1P 477209-28-2P
477209-29-3P 477209-30-6P 477209-31-7P
477209-32-8P 477209-33-9P 477209-34-0P
477209-35-1P 477209-36-2P 477209-37-3P
477209-38-4P 477209-39-5P 477209-40-8P
477209-41-9P 477209-42-0P 477209-43-1P
477209-44-2P 477209-45-3P 477209-47-5P
477209-48-6P 477209-49-7P 477209-50-0P
477209-51-1P 477209-52-2P 477209-54-4P
477209-56-6P 477209-57-7P 477209-59-9P
477209-60-2P 477209-61-3P 477209-62-4P
477209-63-5P 477209-64-6P 477209-65-7P
477209-66-8P 477209-67-9P 477209-68-0P
477209-69-1P 477209-70-4P 477209-71-5P
477209-73-7P 477209-74-8P 477209-75-9P
477209-76-0P 477209-77-1P 477209-78-2P
477209-79-3P 477209-80-6P 477209-81-7P
477209-82-8P 477209-83-9P 477209-84-0P
477209-85-1P 477209-86-2P 477209-87-3P
477209-88-4P 477209-89-5P 477209-90-8P
477209-91-9P 477209-92-0P 477209-93-1P
477209-94-2P 477209-95-3P 477209-96-4P
477209-97-5P 477209-98-6P 477209-99-7P
477210-00-7P 477210-01-8P 477210-02-9P
477210-03-0P 477210-04-1P 477210-05-2P
477210-06-3P 477210-07-4P 477210-08-5P
477210-09-6P 477210-10-9P 477210-11-0P
477210-12-1P 477210-13-2P 477210-14-3P
477210-15-4P 477210-16-5P 477210-17-6P
477210-18-7P 477210-19-8P 477210-20-1P
477210-21-2P 477210-22-3P 477210-23-4P
477210-24-5P 477210-25-6P 477210-26-7P

477210-27-8P 477328-57-7P 477328-58-8P

477328-64-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

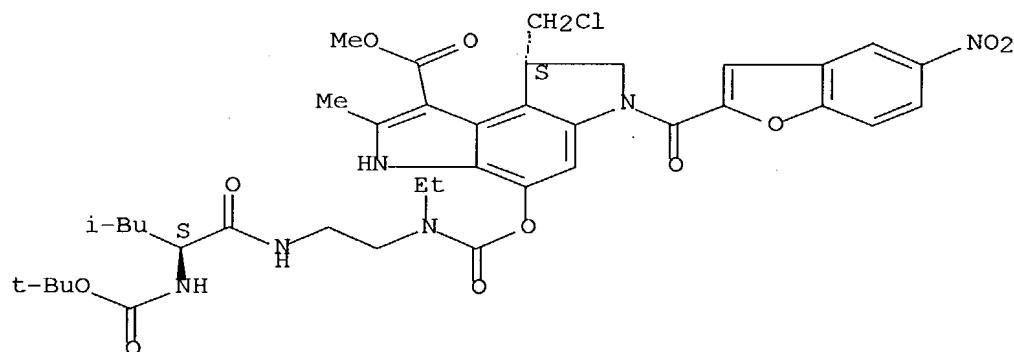
(preparation of duocarmycin analogs as potent cytotoxins)

RN 477207-70-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(7S)-

2-ethyl-11,11-dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



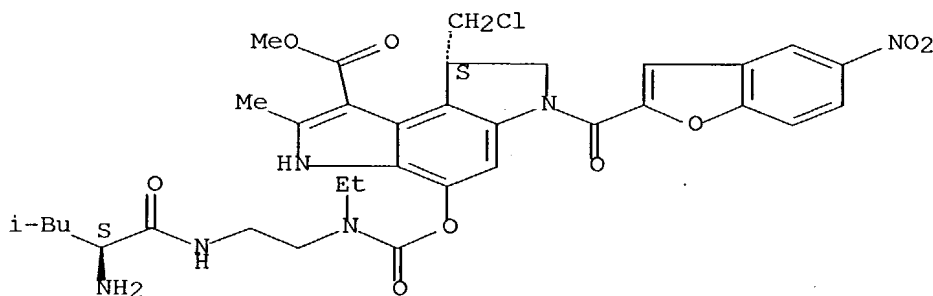
RN 477207-71-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[[2-[[(2S)-2-amino-4-

methyl-1-oxopentyl]amino]ethyl]ethylamino]carbonyl]oxy]-8-(chloromethyl)-

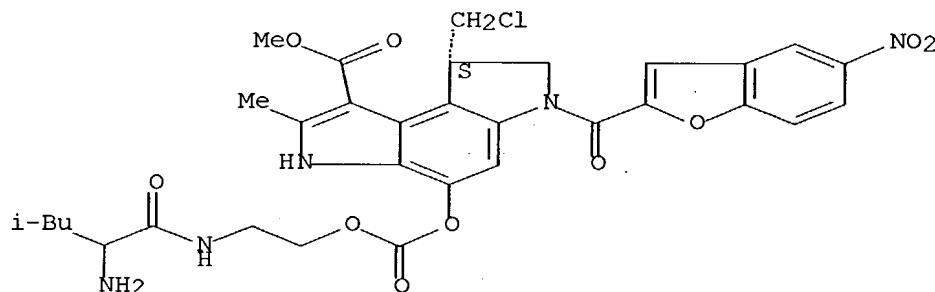
3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



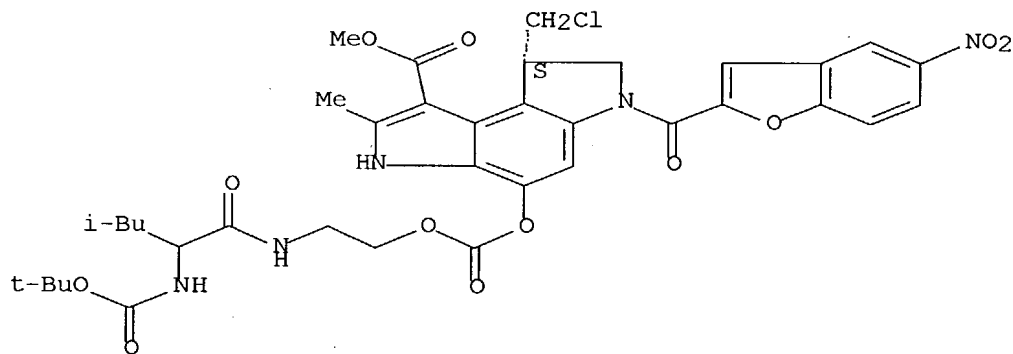
RN 477207-72-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-amino-4-methyl-1-oxopentyl)amino]ethoxy]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-(9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 477207-73-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[11,11-dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-2,10-dioxo-5,8-diazadodec-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

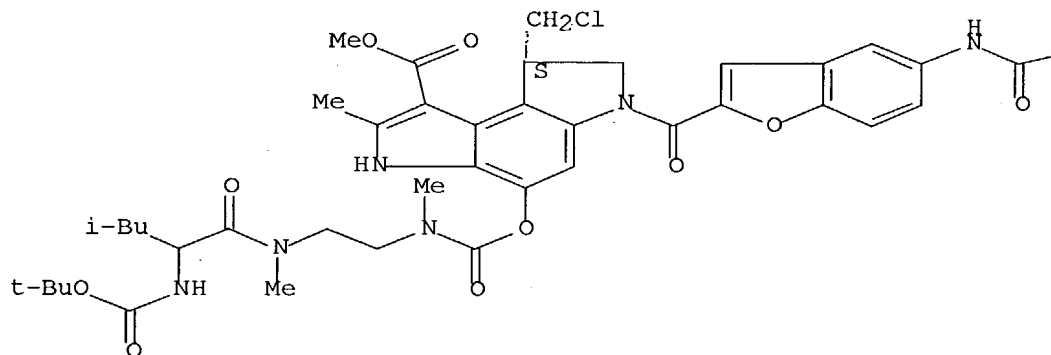


RN 477207-74-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

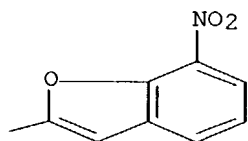
tetrahydro-2-methyl-6-[[5-[[[7-nitro-2-benzofuranyl) carbonyl] amino]-2-benzofuranyl] carbonyl]-4-[[[2,5,11,11-tetramethyl-7-(2-methylpropyl)-1,6,9-trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

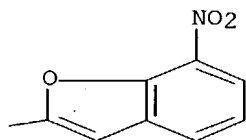
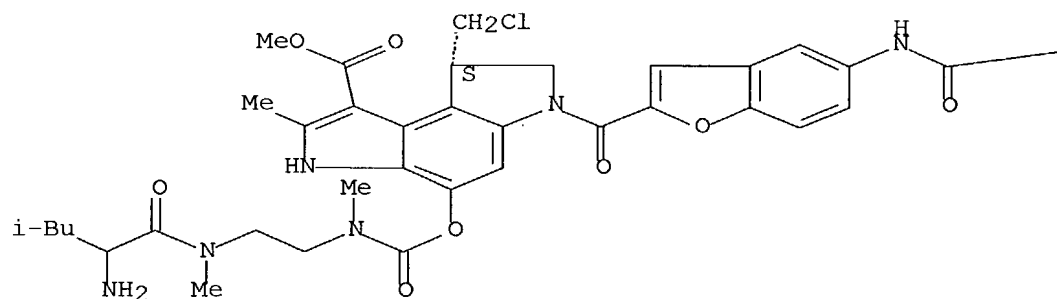


PAGE 1-B



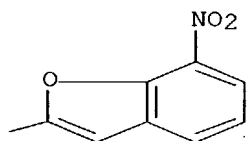
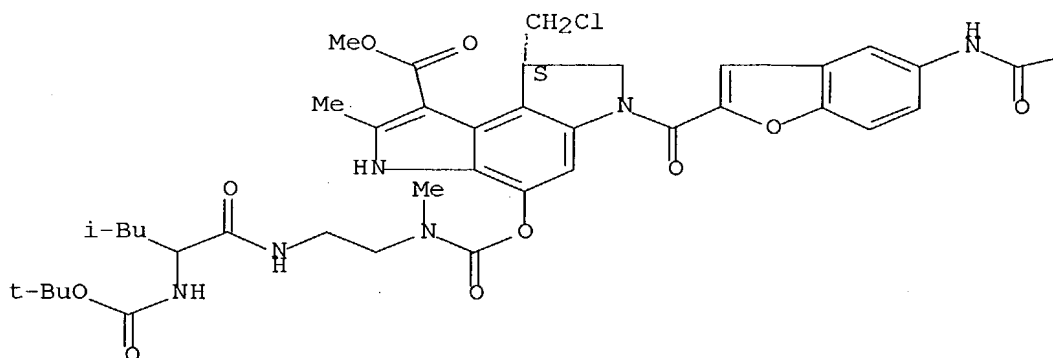
RN 477207-75-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-amino-4-methyl-1-oxopentyl)methylamino]ethyl)methylamino]carbonyl]oxy]-8-(chloromethyl)-
3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[7-nitro-2-benzofuranyl) carbonyl] amino]-2-benzofuranyl] carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



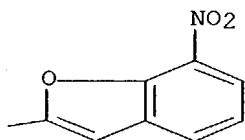
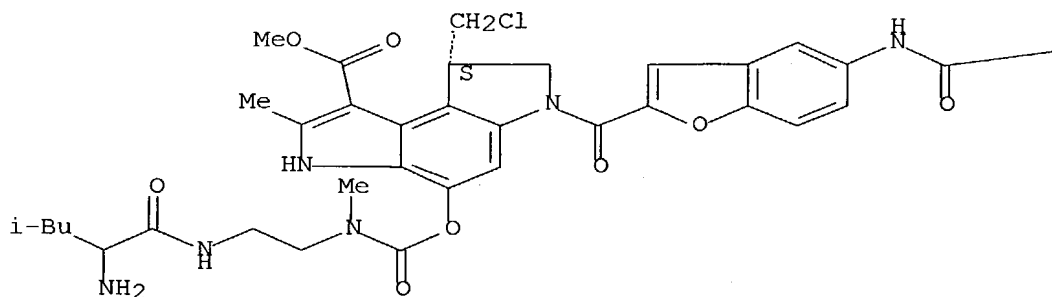
RN 477207-76-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-2-methyl-6-[[5-[[(7-nitro-2-benzofuranyl) carbonyl] amino]-2-
 benzofuranyl] carbonyl]-4-[[2,11,11-trimethyl-7-(2-methylpropyl)-1,6,9-
 trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry.



RN 477207-77-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-amino-4-methyl-1-oxopentyl)amino]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[7-nitro-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

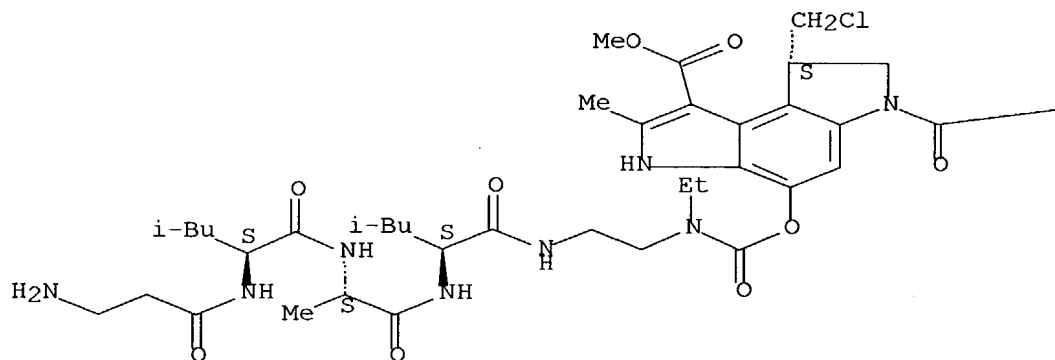
Absolute stereochemistry.



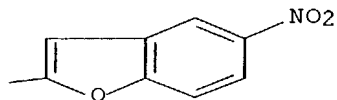
RN 477207-78-6 CAPLUS

CN L-Leucinamide, β -alanyl-L-leucyl-L-alanyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

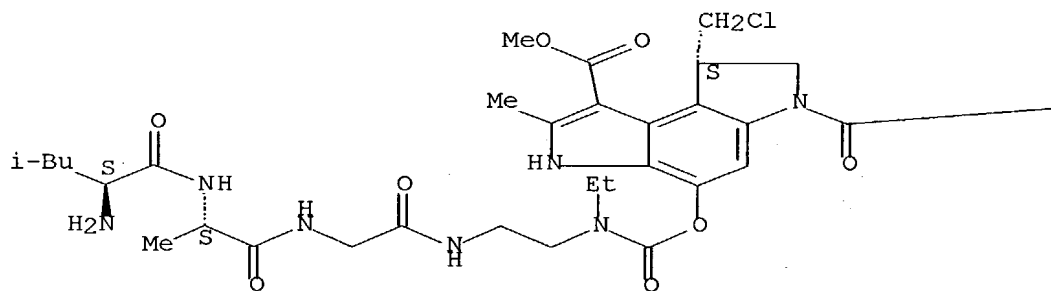


RN 477207-79-7 CAPLUS

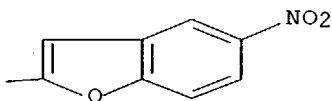
CN Glycinamide, L-leucyl-L-alanyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



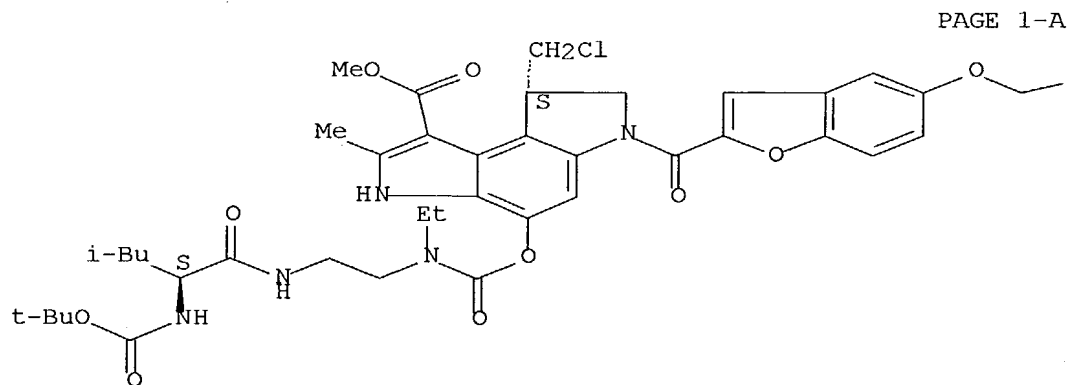
PAGE 1-B



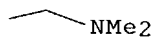
RN 477207-80-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[(7S)-2-ethyl-11,11-dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



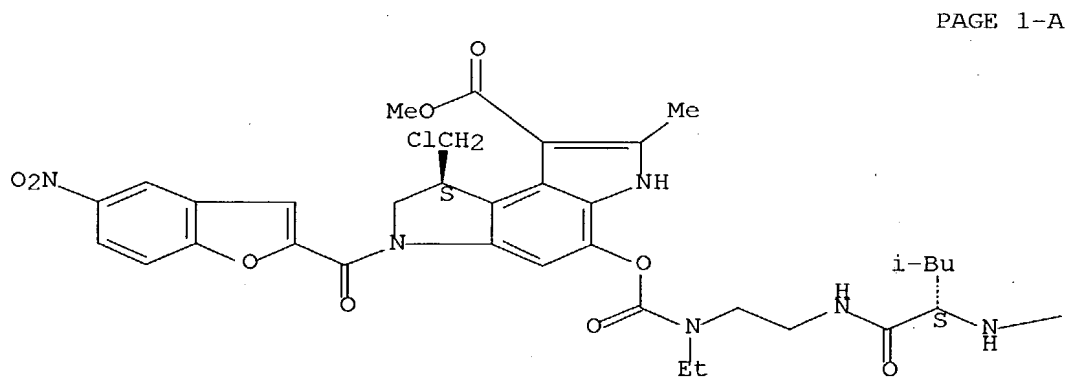
PAGE 1-B



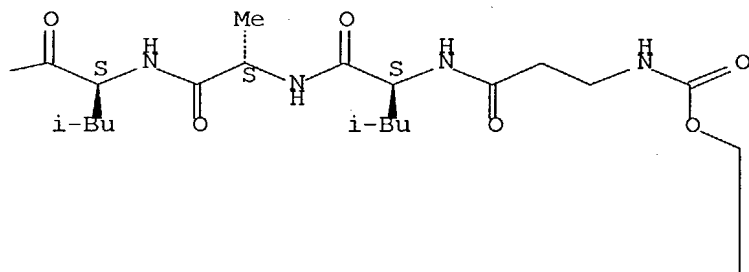
RN 477207-81-1 CAPLUS

CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

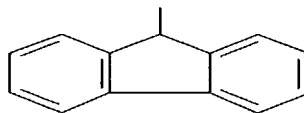
Absolute stereochemistry.



PAGE 1-B



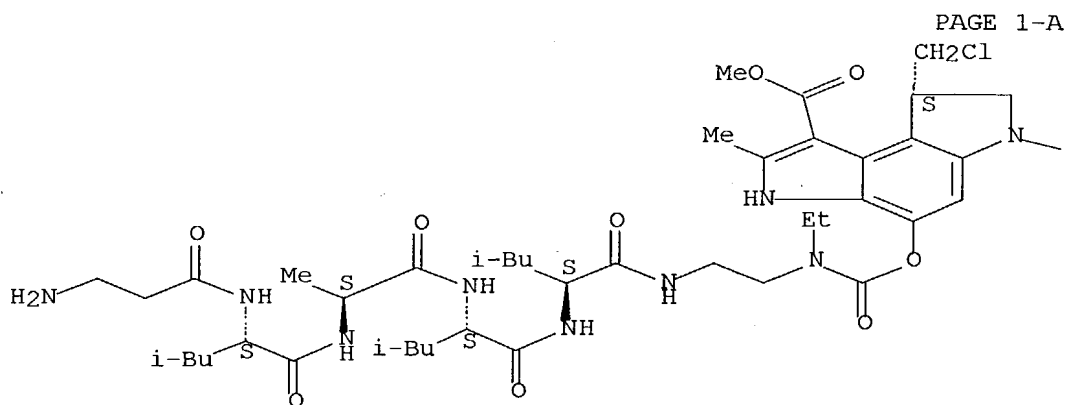
PAGE 2-B



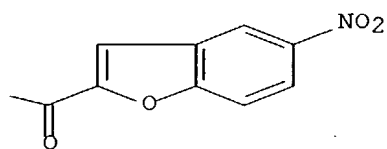
RN 477207-82-2 CAPLUS

CN L-Leucinamide, β -alanyl-L-leucyl-L-alanyl-L-leucyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



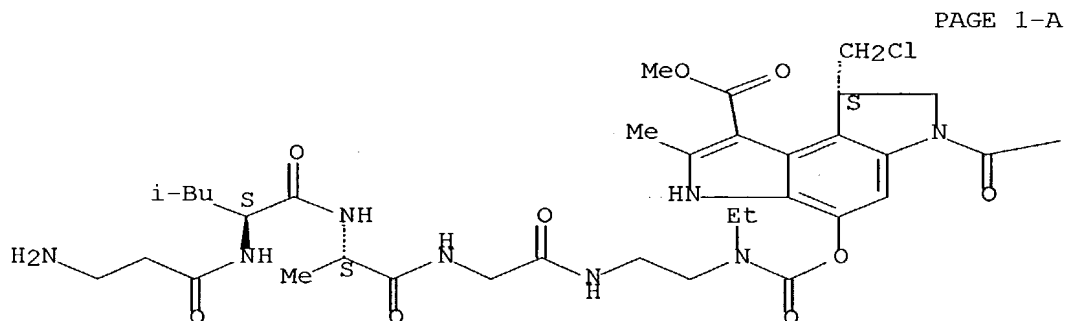
PAGE 1-B

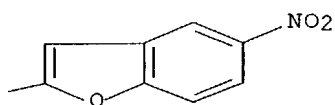


RN 477207-83-3 CAPLUS

CN Glycinamide, β -alanyl-L-leucyl-L-alanyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

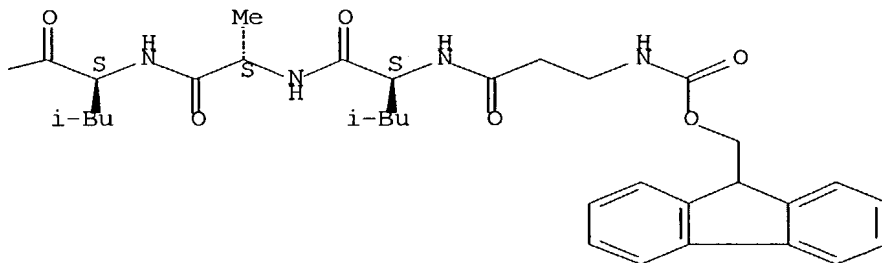
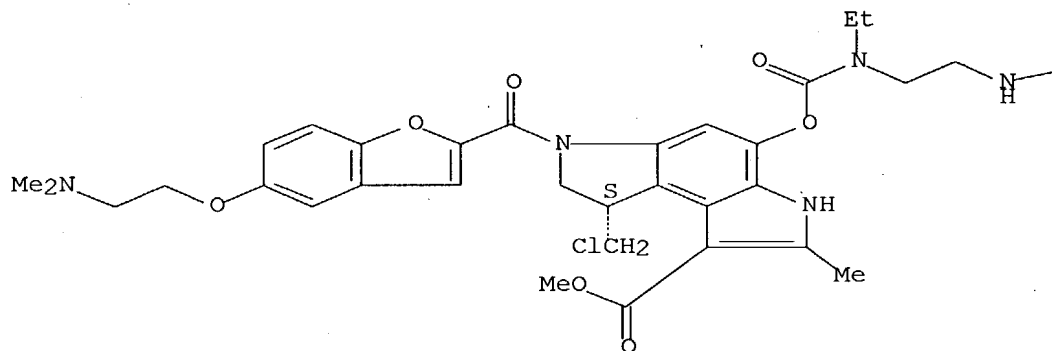




RN 477207-84-4 CAPLUS

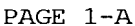
CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy) carbonyl]- β -alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477207-85-5 CAPLUS

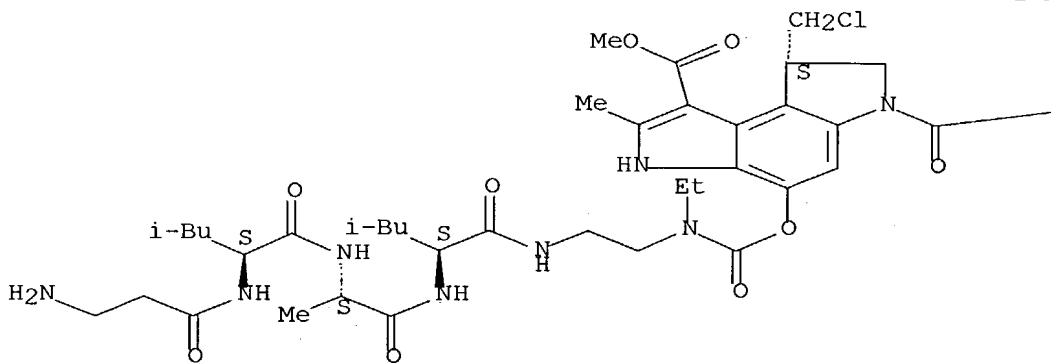
Absolute stereochemistry.

 —NMe_2

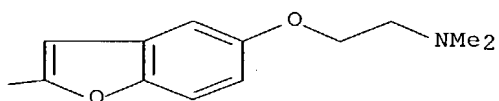
CN L-Leucinamide, β -alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

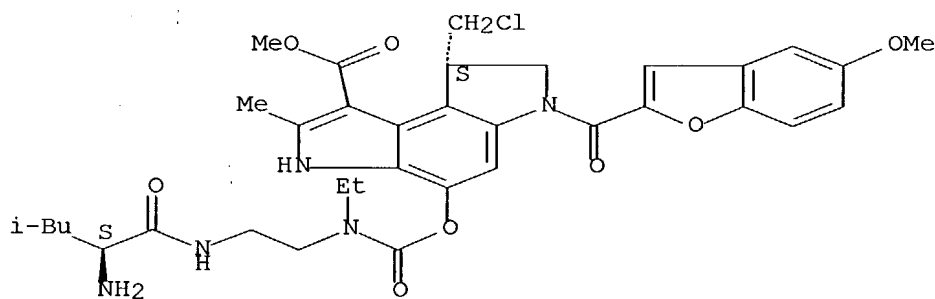


PAGE 1-B



RN 477207-87-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[[[(2S)-2-amino-4-methyl-1-oxopentyl]amino]ethyl]ethylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

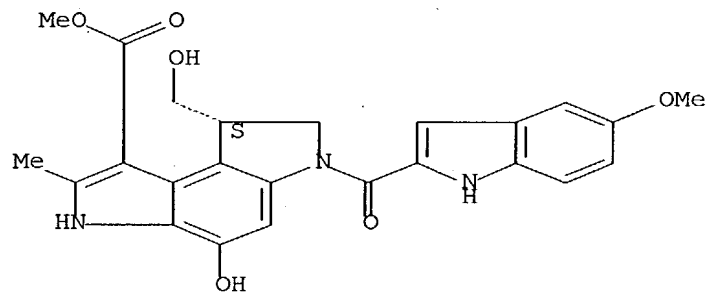
Absolute stereochemistry.



RN 477207-92-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-4-

hydroxy-8-(hydroxymethyl)-6-[(5-methoxy-1H-indol-2-yl) carbonyl]-2-methyl-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

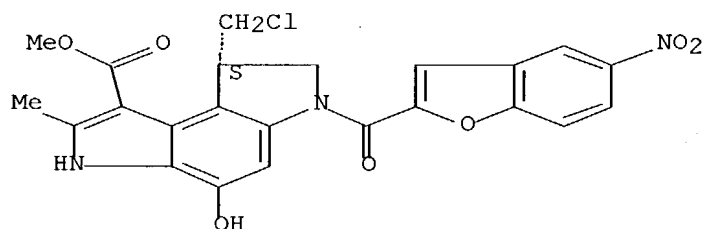
Absolute stereochemistry.



RN 477207-95-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5-nitro-2-benzofuranyl) carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

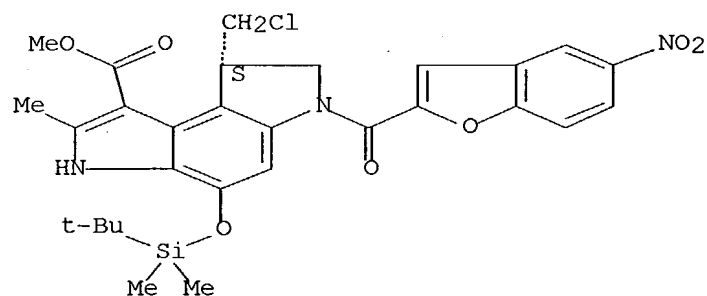
Absolute stereochemistry.



RN 477207-96-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl) carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

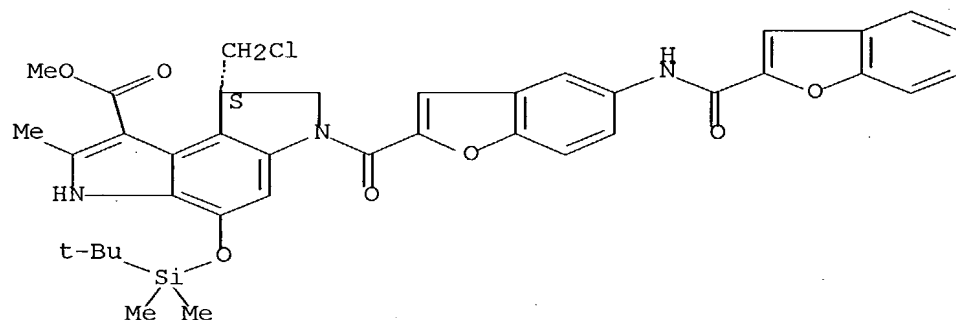
Absolute stereochemistry.



RN 477207-97-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

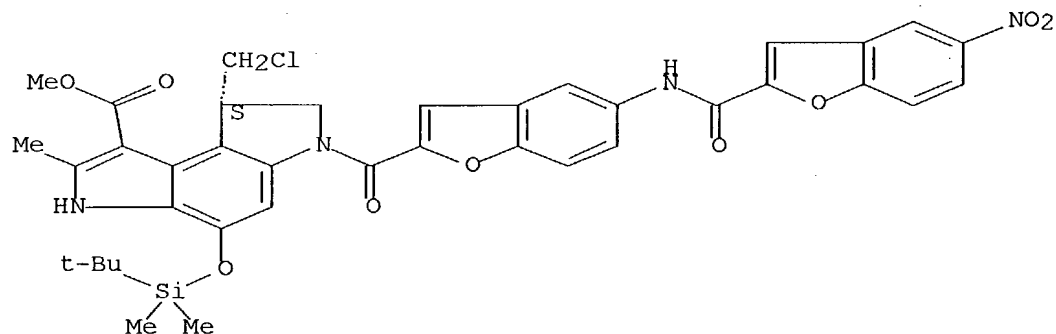
Absolute stereochemistry.



RN 477207-99-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[(5-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

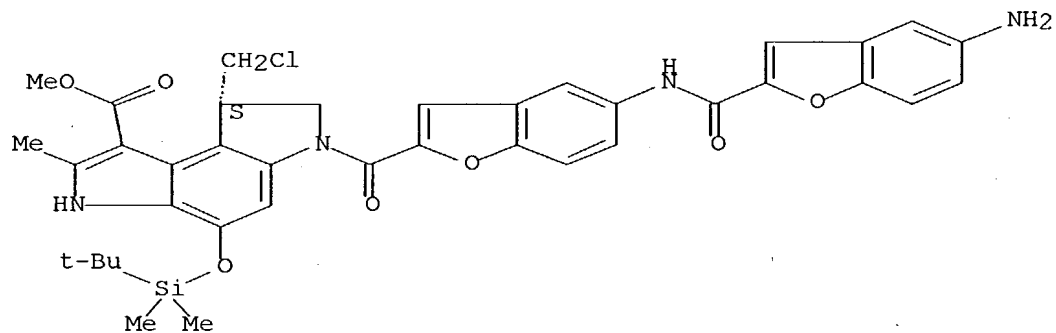
Absolute stereochemistry.



RN 477208-00-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[5-amino-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

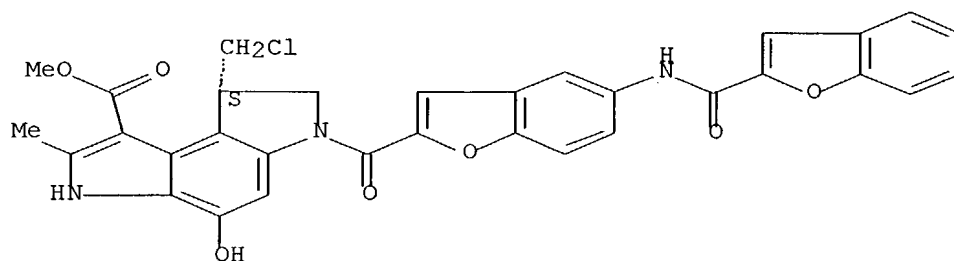
Absolute stereochemistry.



RN 477208-02-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

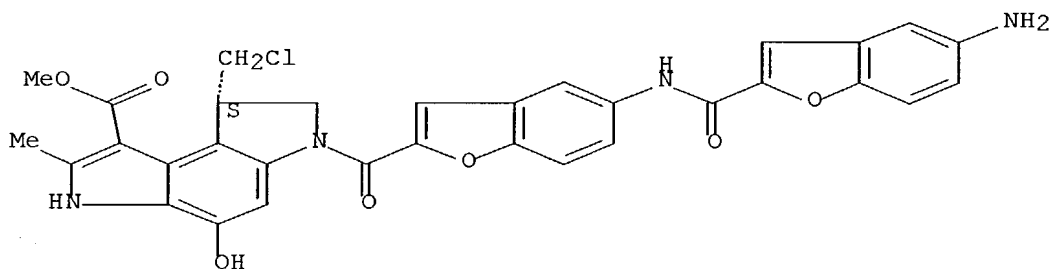
Absolute stereochemistry.



RN 477208-04-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[5-amino-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

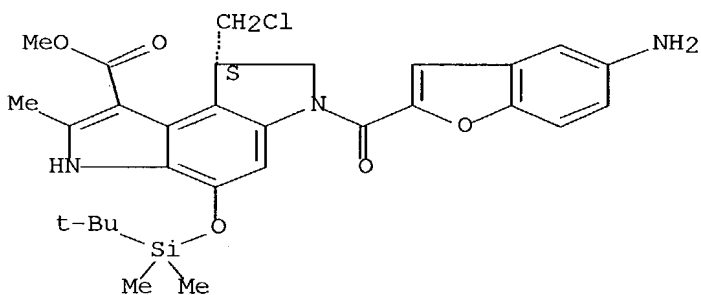
Absolute stereochemistry.



RN 477208-05-2 CAPLUS

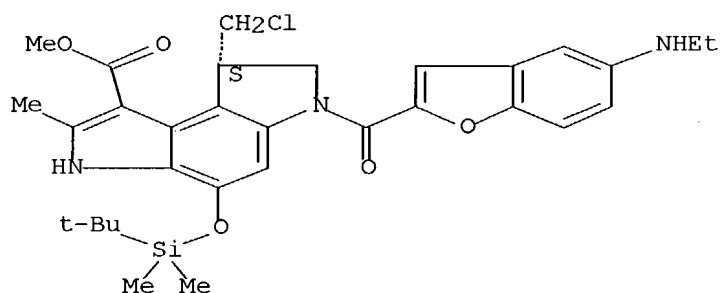
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



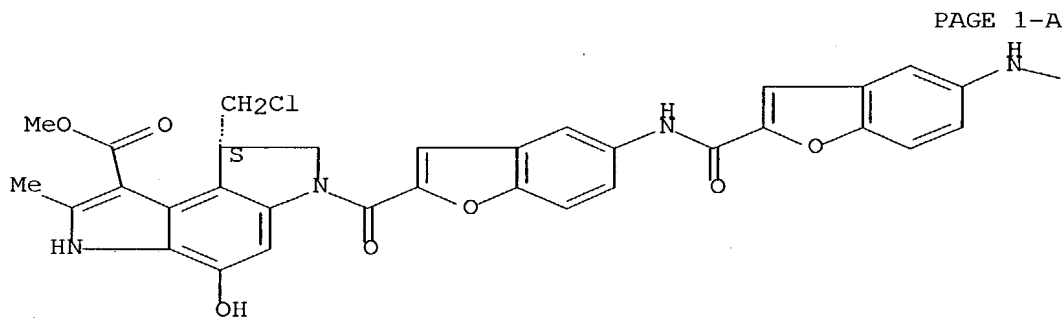
RN 477208-07-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-6-[[5-(ethylamino)-2-
 benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

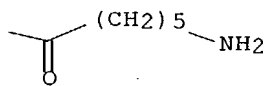


RN 477208-08-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[(6-amino-1-
 oxohexyl)amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-
 8-
 (chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester,
 (8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A



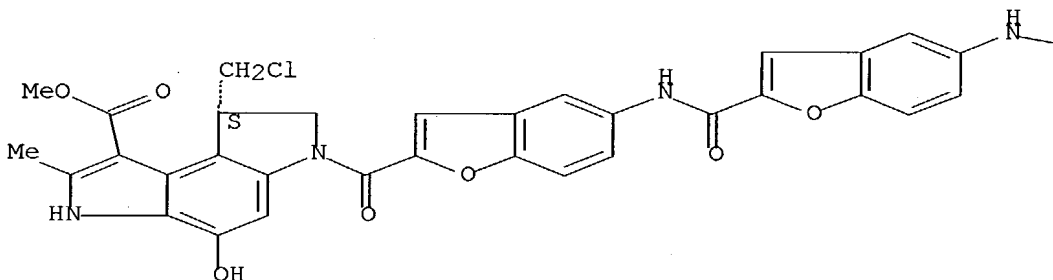
PAGE 1-B

RN 477208-09-6 CAPLUS

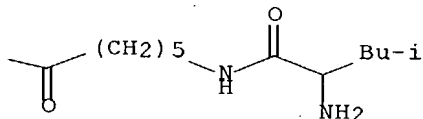
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[6-[(2-amino-4-methyl-1-oxopentyl)amino]-1-oxohexyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



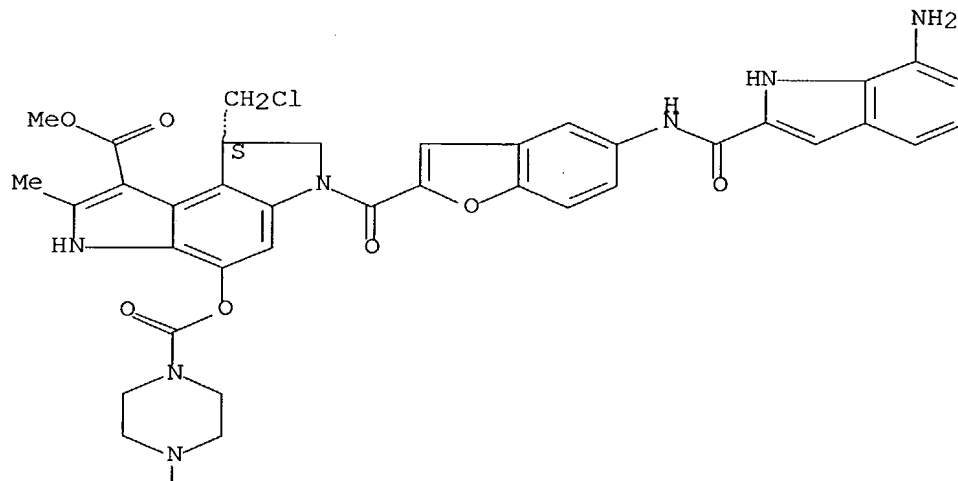
PAGE 1-B



RN 477208-10-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-amino-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

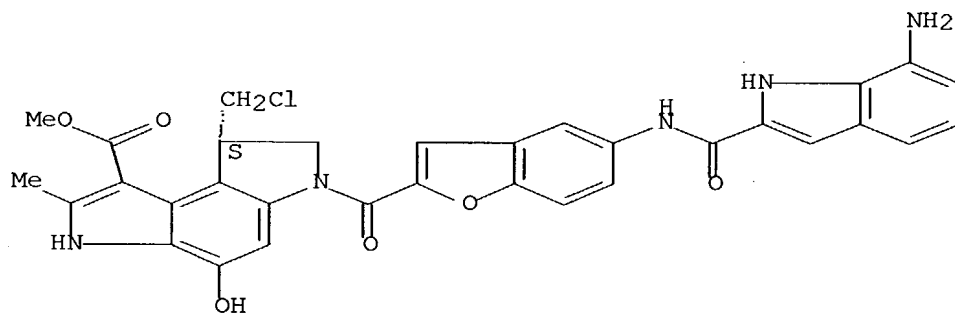
Absolute stereochemistry.



Me

RN 477208-11-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[(7-amino-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

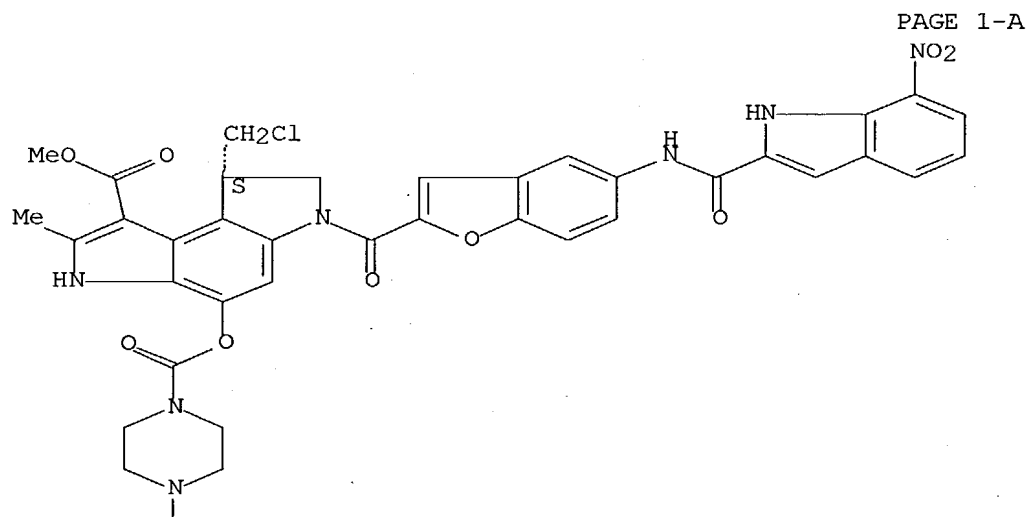


RN 477208-12-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-

3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[[5-nitro-1H-indol-2-yl) carbonyl]amino]-2-benzofuranyl] carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 2-A

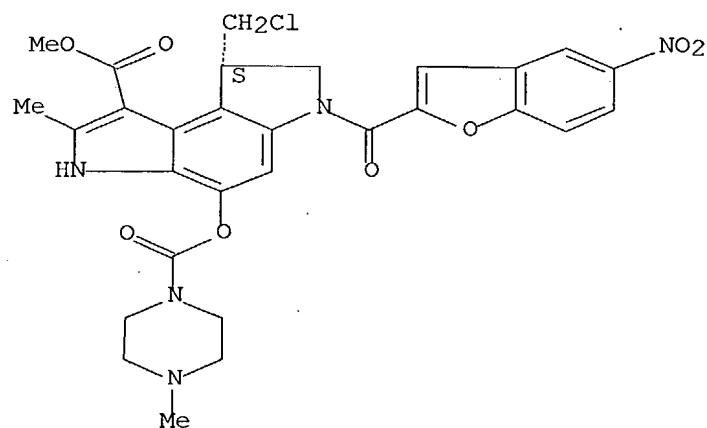
Me

RN 477208-13-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

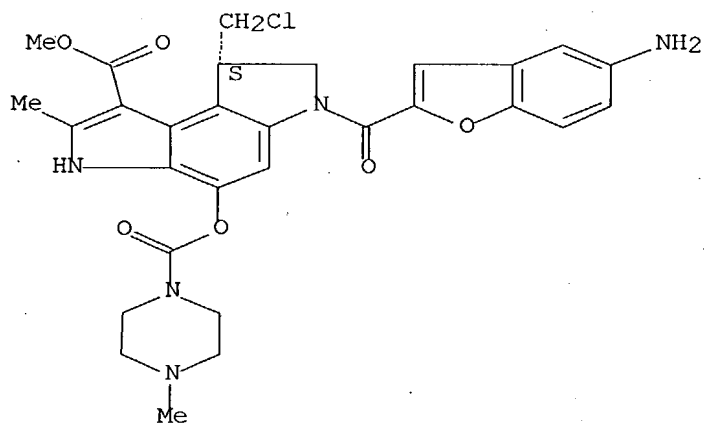
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[[5-nitro-2-benzofuranyl) carbonyl]amino]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



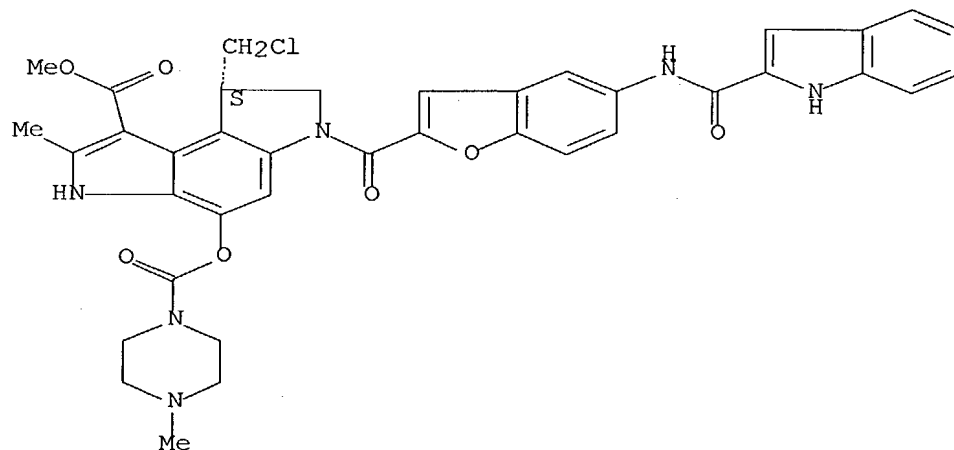
RN 477208-14-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



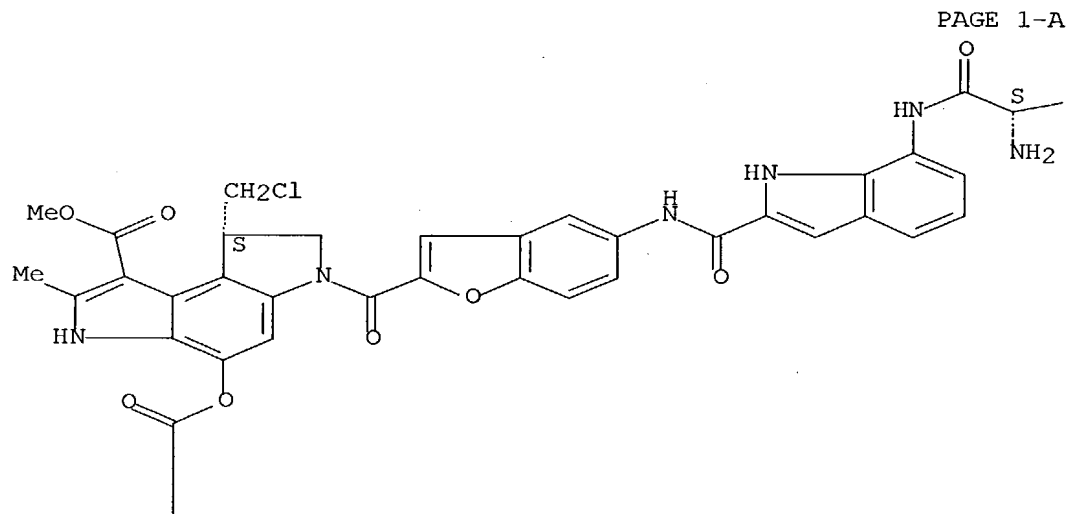
RN 477208-18-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-2-benzofuranyl]carbonyl]-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

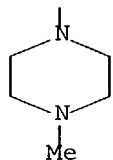


RN 477208-21-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[(2S)-2-amino-4-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

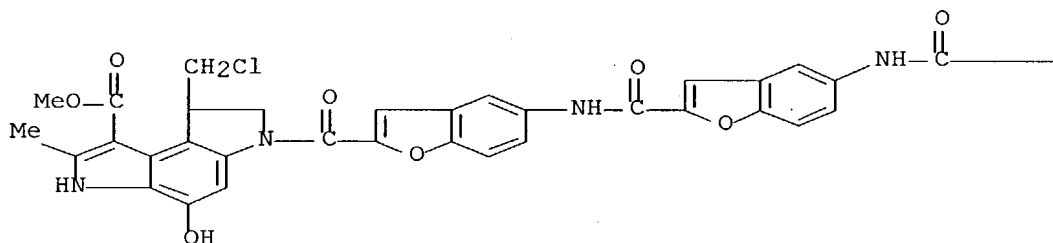
Absolute stereochemistry.



— Bu-i



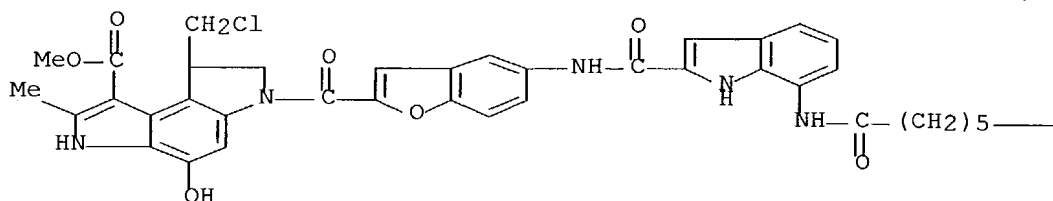
RN 477208-22-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[(6-amino-1-oxohexyl)amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester
 (9CI)
 (CA INDEX NAME)

— (CH₂)₅—NH₂

RN 477208-23-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[(6-amino-1-oxohexyl)amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester
 (9CI)

(CA INDEX NAME)

PAGE 1-A



PAGE 1-B

—NH₂

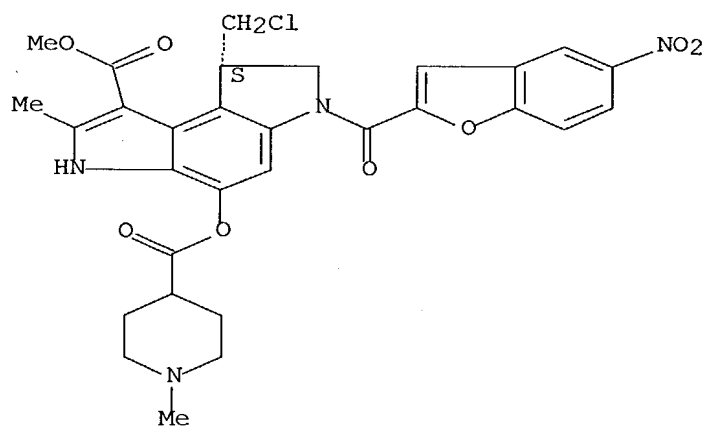
RN 477208-24-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-methyl-4-piperidinyl)carbonyl]oxy]-6-[(5-nitro-

2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

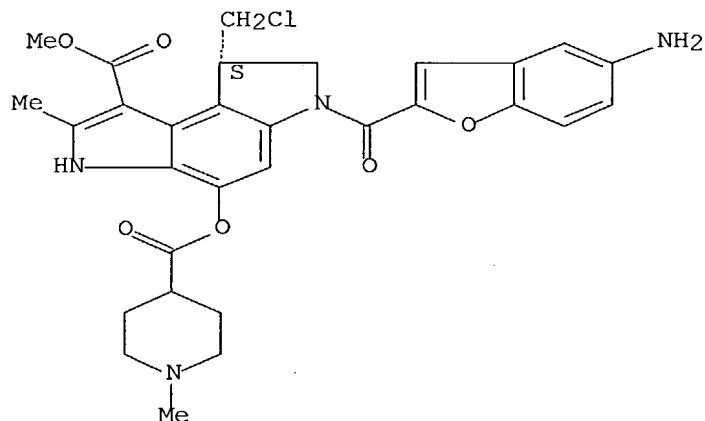


RN 477208-25-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-

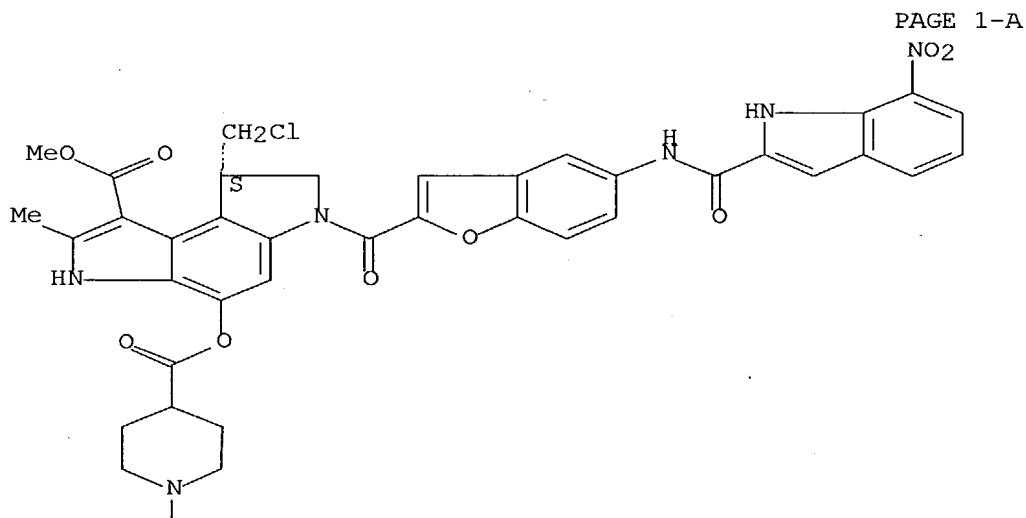
[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477208-26-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-6-[[5-nitro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

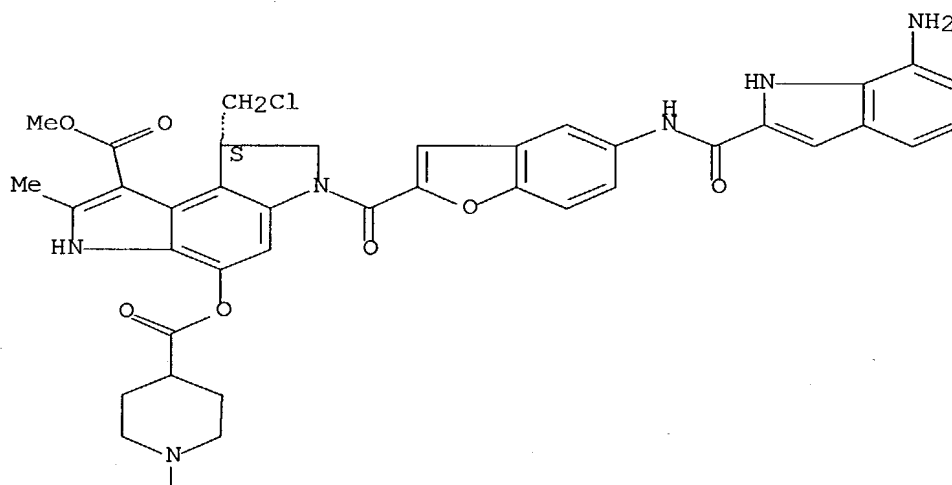


PAGE 1-A

Me

RN 477208-27-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[(7-amino-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methyl-4-piperidiny]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

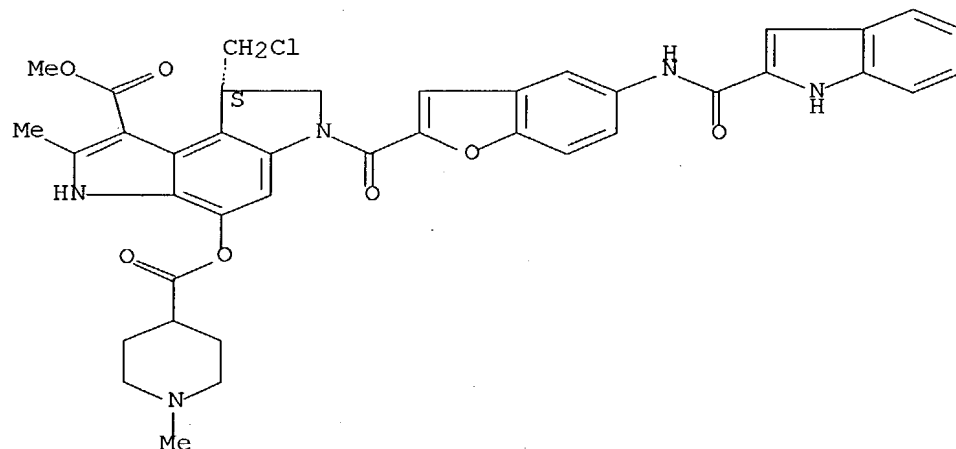


Me

RN 477208-28-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-2-benzofuranyl]carbonyl]-2-methyl-4-[[[(1-methyl-4-piperidiny]carbonyl]oxy]-, methyl ester, (8S)-

(9CI) (CA INDEX NAME)

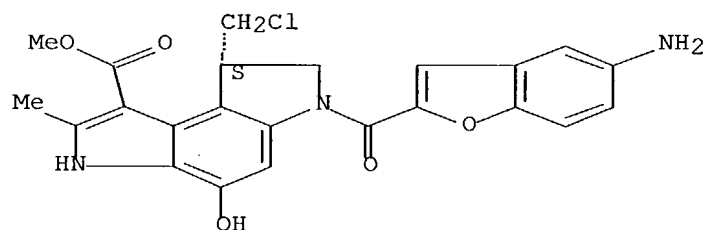
Absolute stereochemistry.



RN 477208-32-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

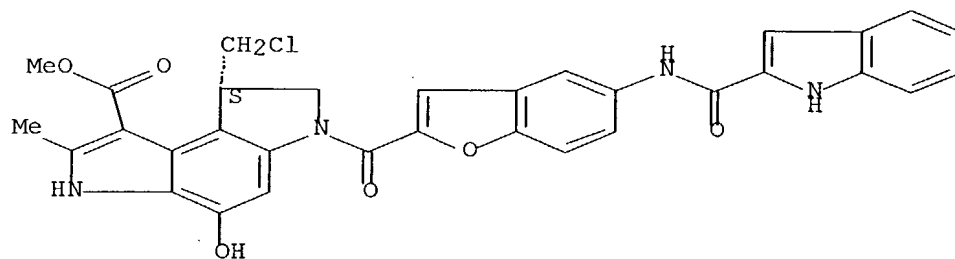
Absolute stereochemistry.



RN 477208-33-6 CAPLUS

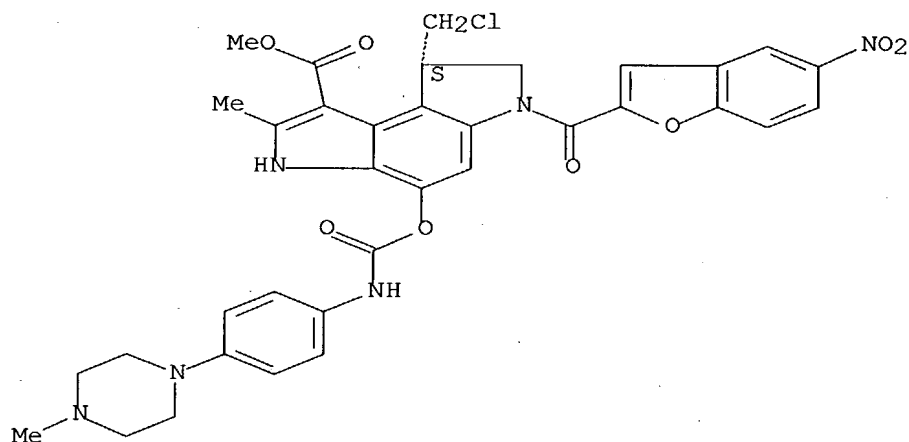
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



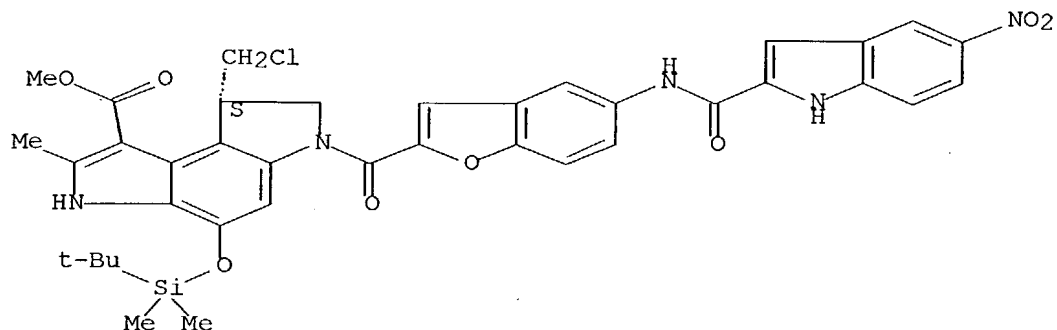
RN 477208-34-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-2-methyl-4-[[[4-(4-methyl-1-
 piperazinyl)phenyl]amino]carbonyl]
 oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry.



RN 477208-39-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[5-
 nitro-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl
 ester, (8S)- (9CI) (CA INDEX NAME)

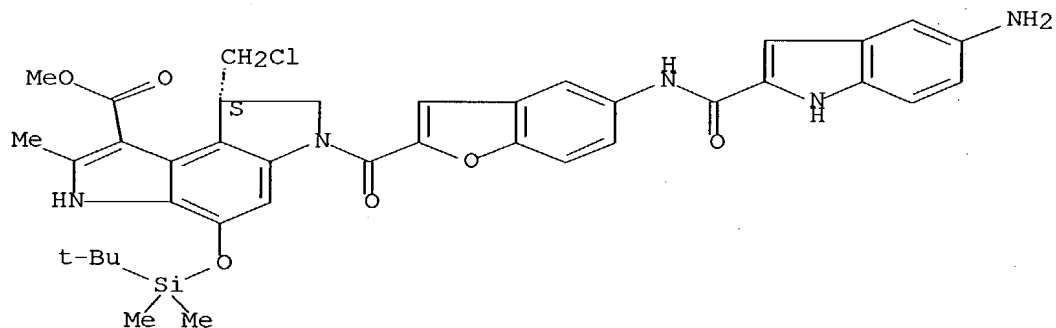
Absolute stereochemistry.



RN 477208-40-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[5-amino-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

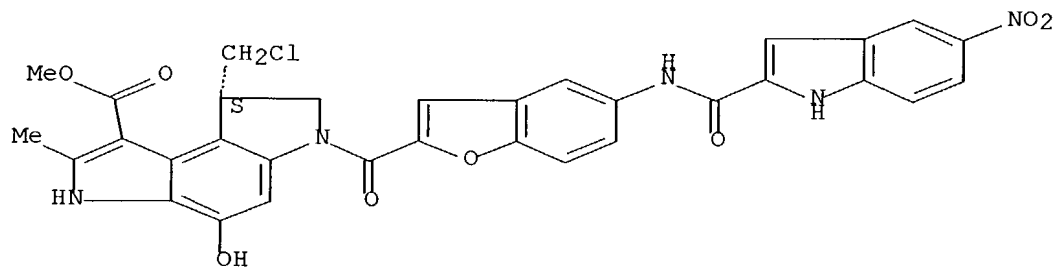
Absolute stereochemistry.



RN 477208-41-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[[5-[[5-nitro-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

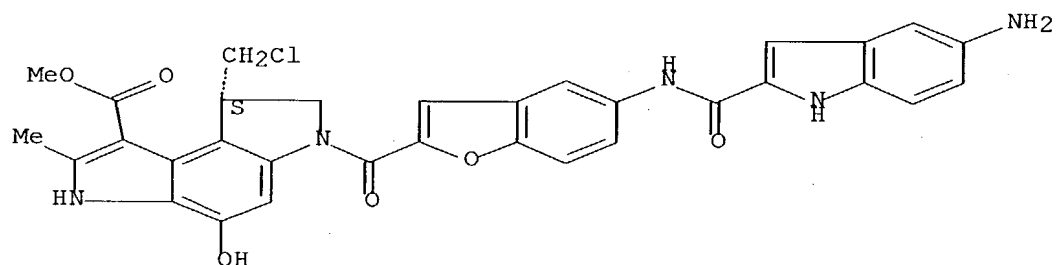
Absolute stereochemistry.



RN 477208-42-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[5-amino-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

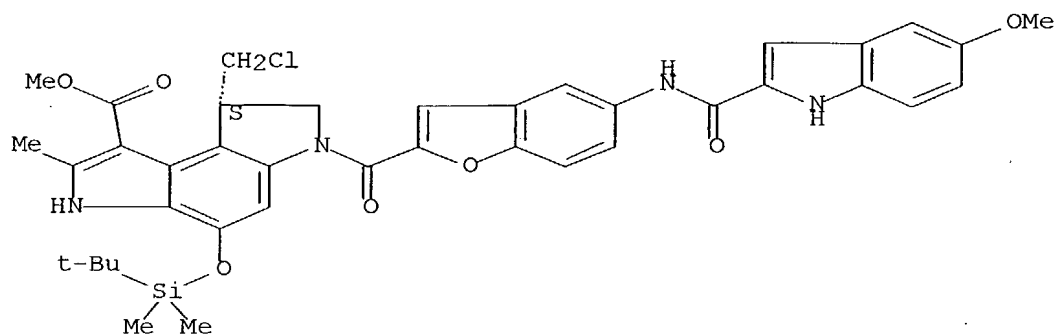
Absolute stereochemistry.



RN 477208-43-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[5-methoxy-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

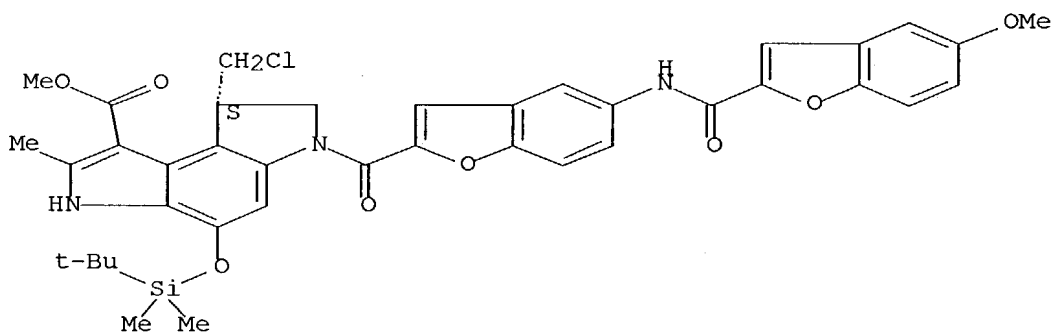
Absolute stereochemistry.



RN 477208-44-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[5-methoxy-
 2-
 benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl
 ester, (8S)- (9CI) (CA INDEX NAME)

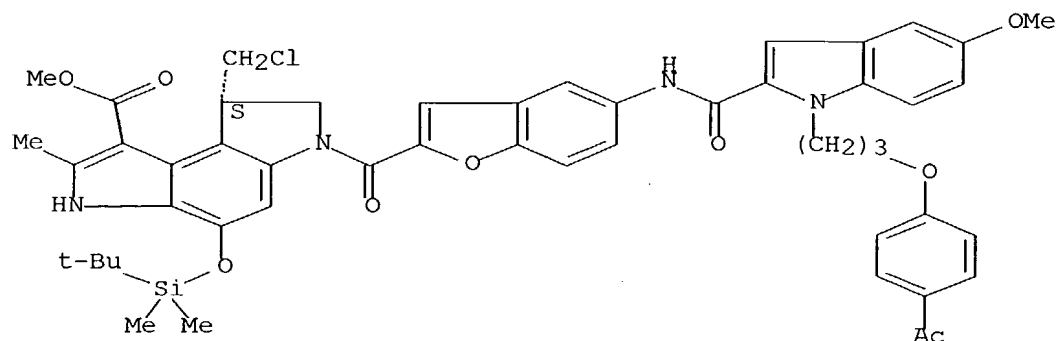
Absolute stereochemistry.



RN 477208-45-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[1-[3-(4-
 acetylphenoxy)propyl]-5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-
 benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[1,1-
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl
 ester, (8S)- (9CI) (CA INDEX NAME)

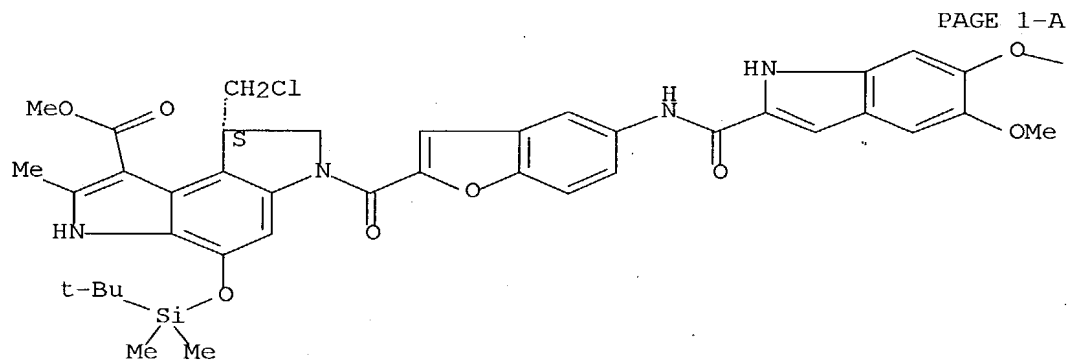
Absolute stereochemistry.



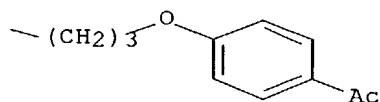
RN 477208-46-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[6-[3-(4-acetylphenoxy)propoxy]-5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A



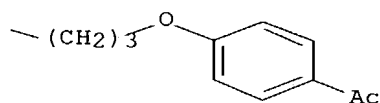
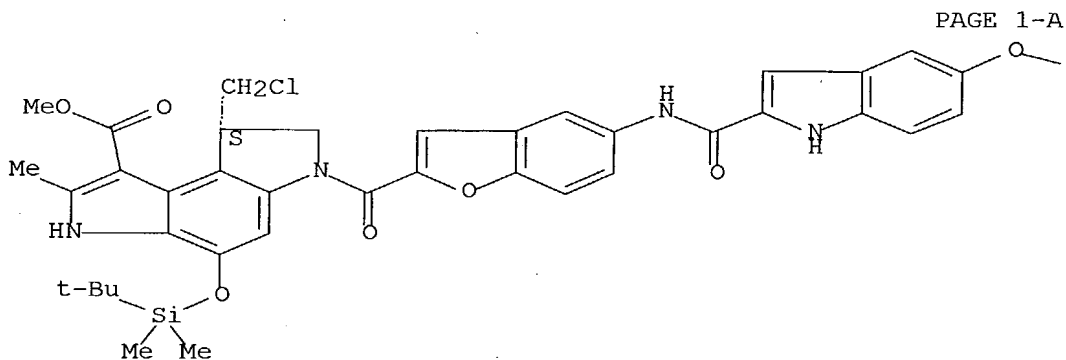
PAGE 1-B

RN 477208-47-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[3-(4-acetylphenoxy)propoxy]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl

ester, (8S)- (9CI) (CA INDEX NAME)

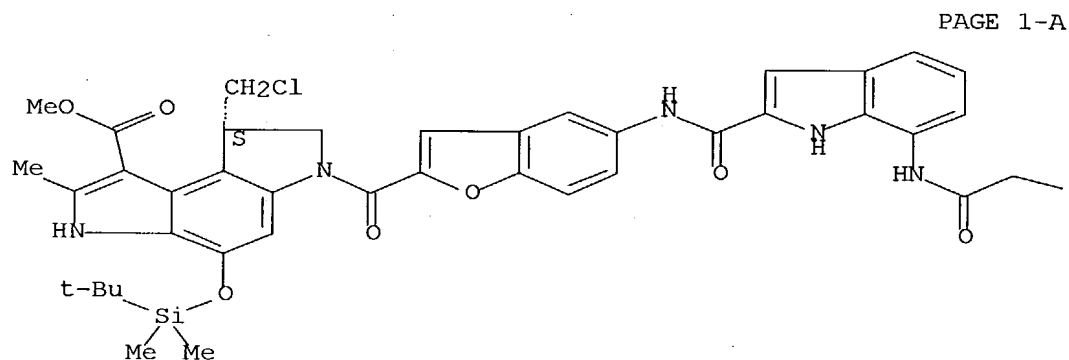
Absolute stereochemistry.



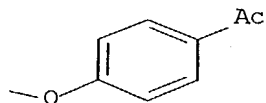
RN 477208-48-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[[4-acetylphenoxy)acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B

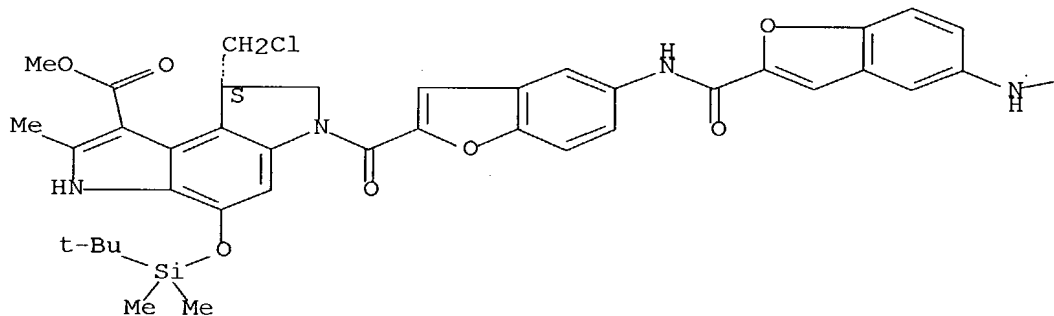


RN 477208-49-4 CAPLUS

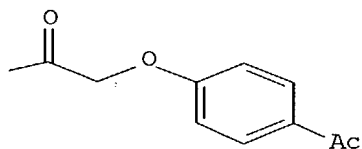
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[4-acetylphenoxy)acetyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



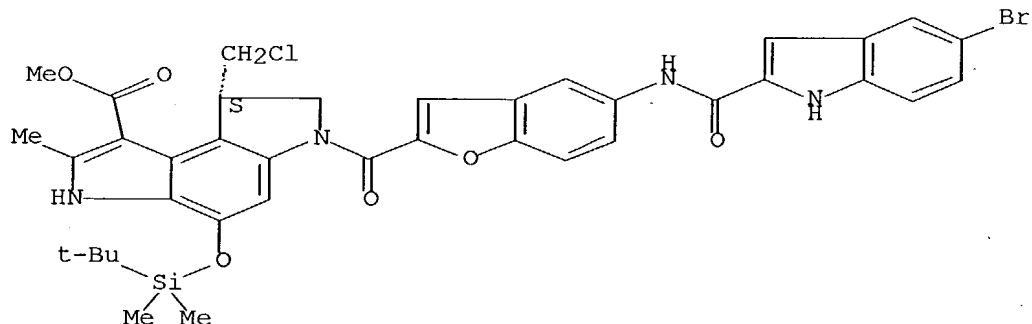
RN 477208-50-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-bromo-1H-

indol-

2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

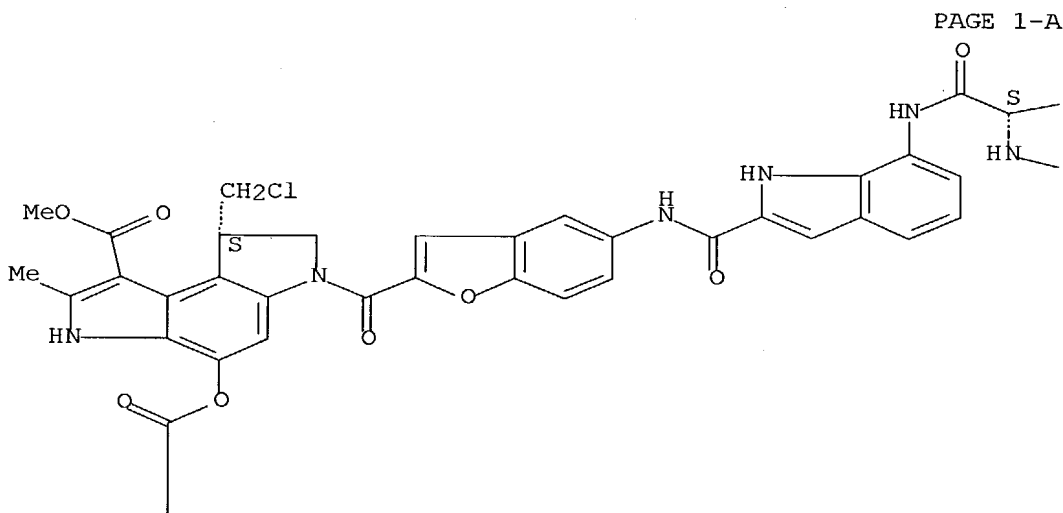


RN 477208-51-8 CAPLUS

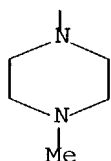
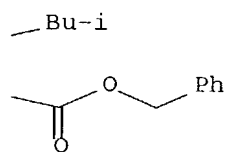
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-6-[[5-[[[7-[(2S)-4-methyl-1-oxo-2-[[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

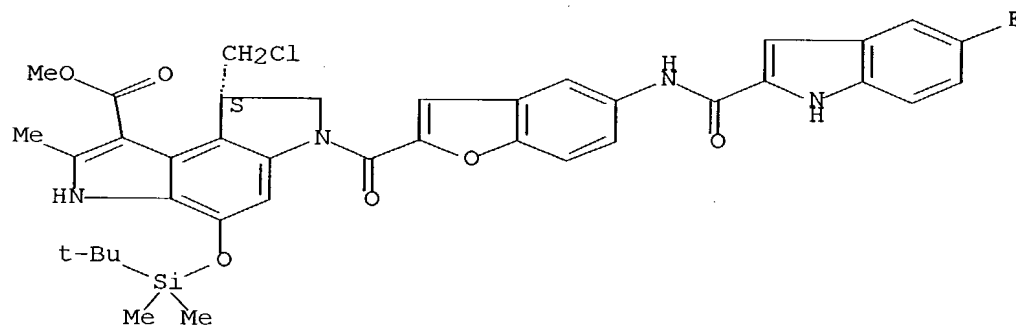


PAGE 1-A



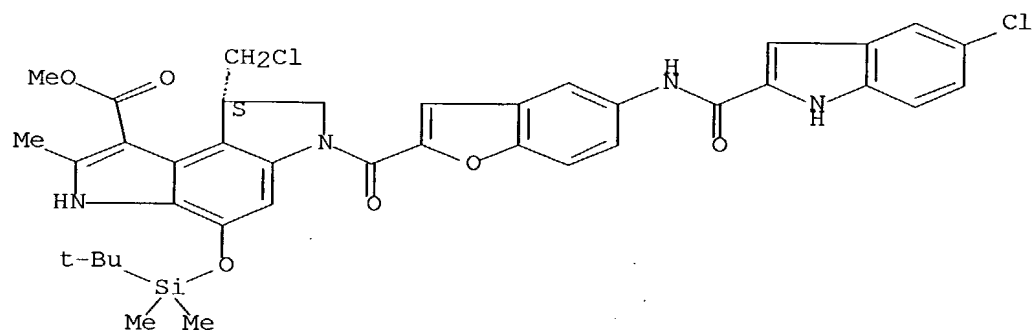
RN 477208-52-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-[[5-(5-fluoro-1H-indol-2-
 yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



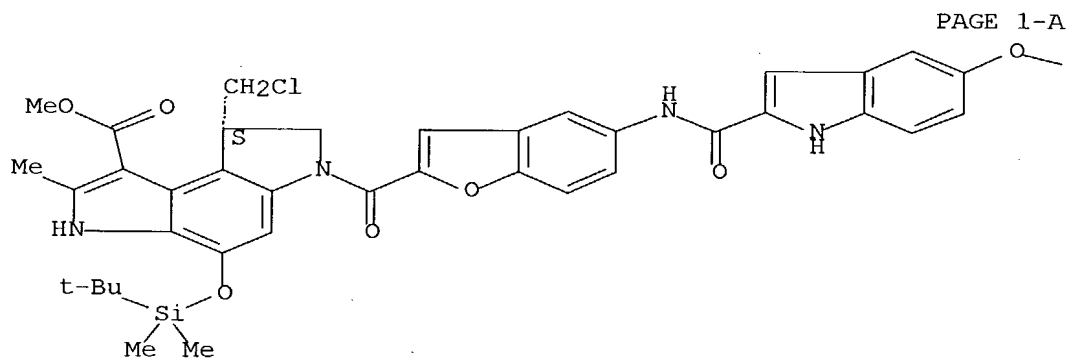
RN 477208-53-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[5-(5-chloro-1H-
 indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[1,1-
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl
 ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477208-54-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[[5-
 (trifluoromethoxy)-1H-indol-2-yl]carbonyl]amino]-2-
 benzofuranyl]carbonyl]-
 , methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

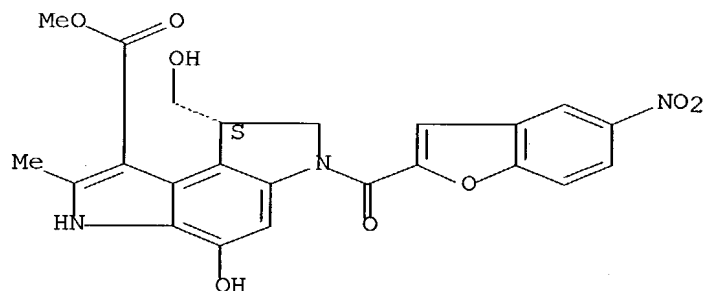
PAGE 1-B

—CF₃

RN 477208-55-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-4-
 hydroxy-8-(hydroxymethyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-

methyl ester, (8S)- (9CI) (CA INDEX NAME)

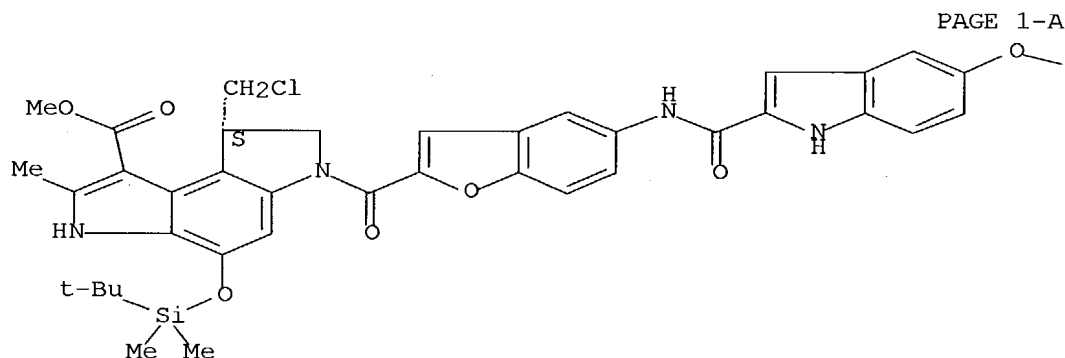
Absolute stereochemistry.



RN 477208-56-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[5-
(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A



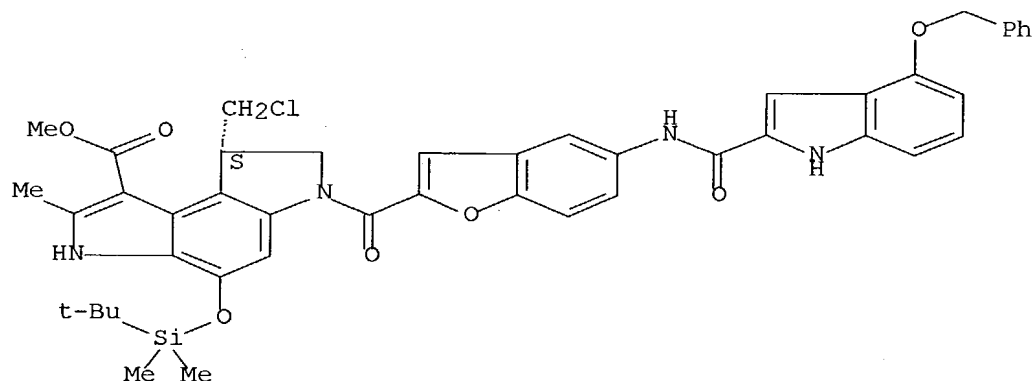
PAGE 1-B

RN 477208-57-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[4-
(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-,

methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



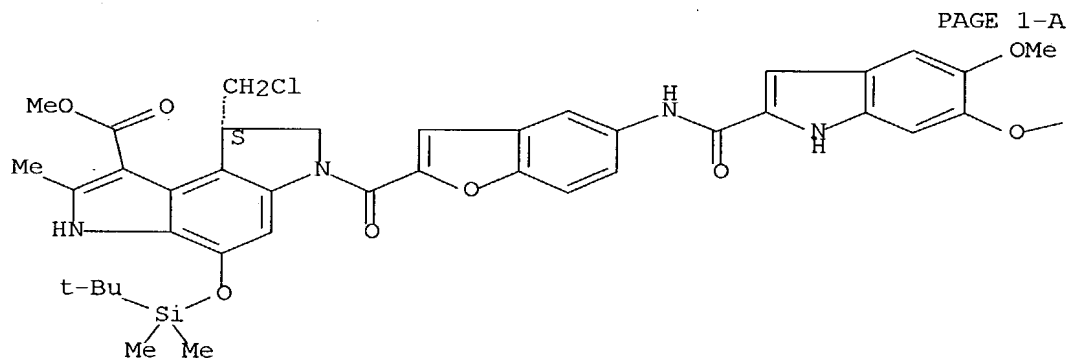
RN 477208-58-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[5-methoxy-
6-
(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-

2-
methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

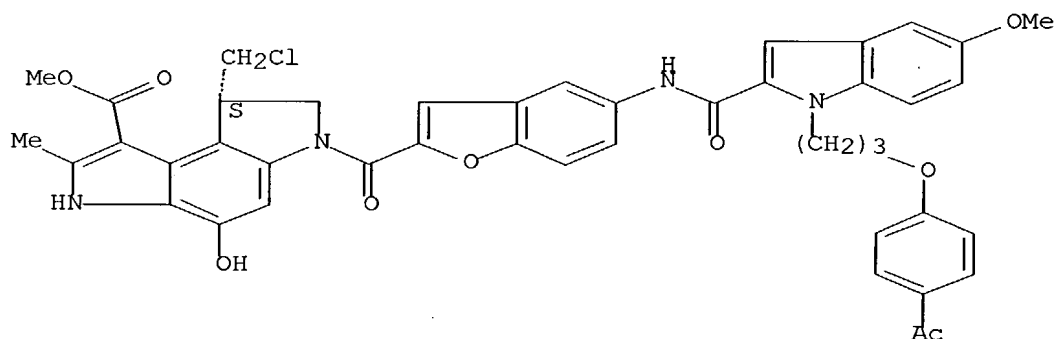
PAGE 1-B

Ph

RN 477208-59-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[1-[3-(4-acetylphenoxy)propyl]-5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

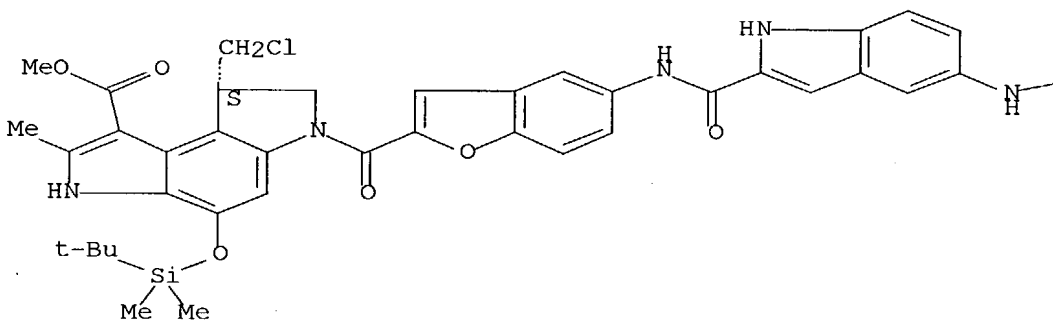
Absolute stereochemistry.



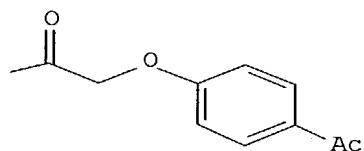
RN 477208-60-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[[4-acetylphenoxy]acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

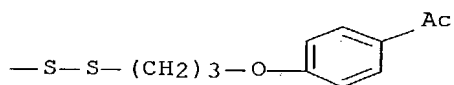
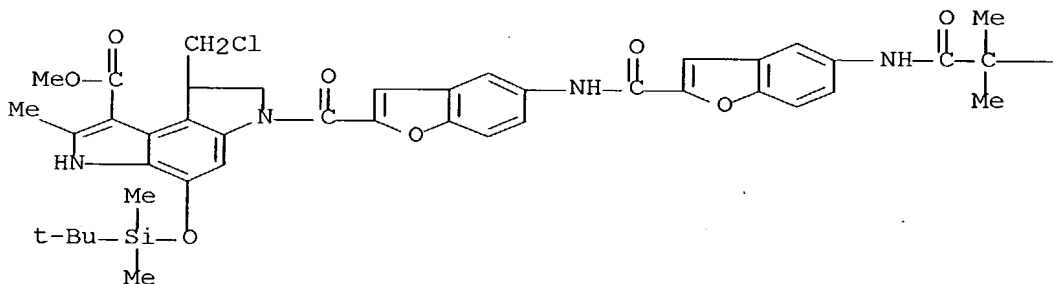


PAGE 1-A



RN 477208-61-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[2-[[3-(4-acetylphenoxy)propyl]dithio]-2-methyl-1-oxopropyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

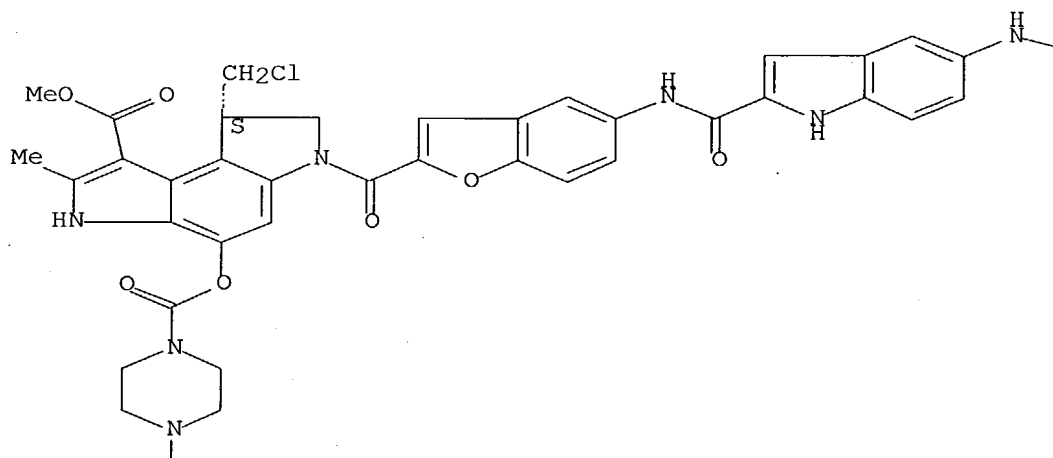


RN 477208-62-1 CAPLUS

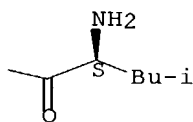
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[2S)-2-amino-4-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

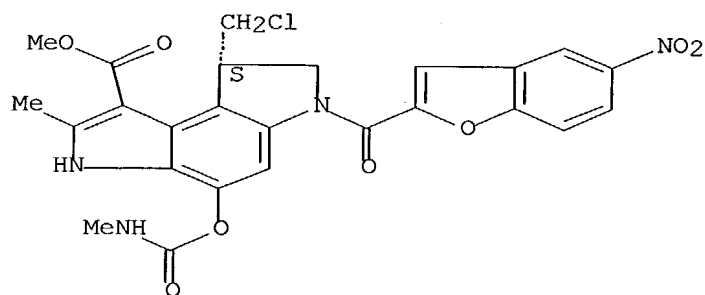


PAGE 2-A



RN 477208-63-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-2-methyl-4-[[(methylamino)carbonyl]oxy]-6-[(5-nitro-2-
benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

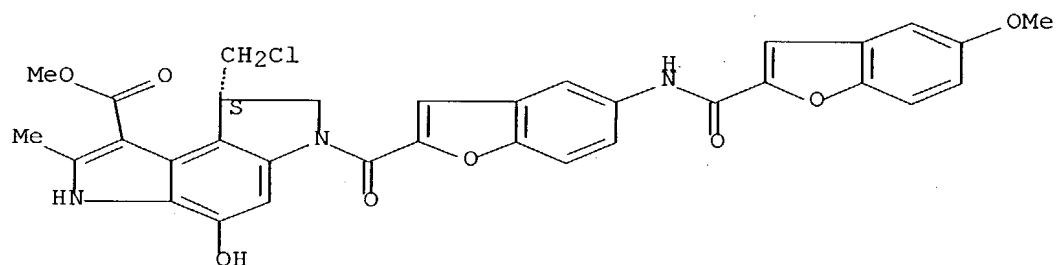


RN 477208-64-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-methyl-6-[[5-[[5-methoxy-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

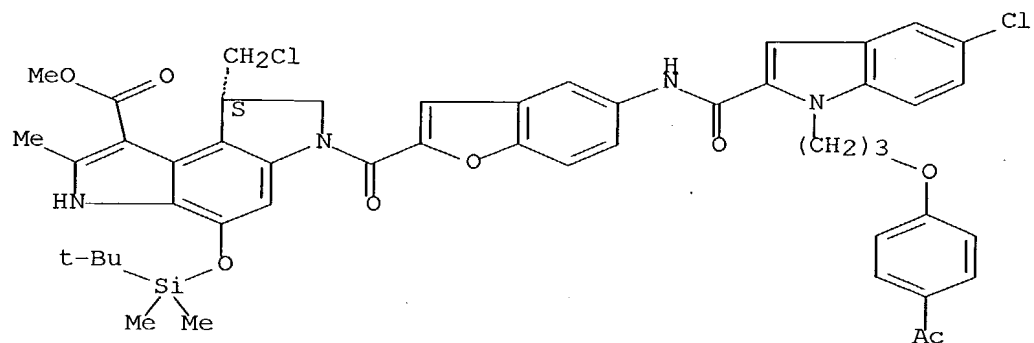
Absolute stereochemistry.



RN 477208-65-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[1-[3-(4-acetylphenoxy)propyl]-5-chloro-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

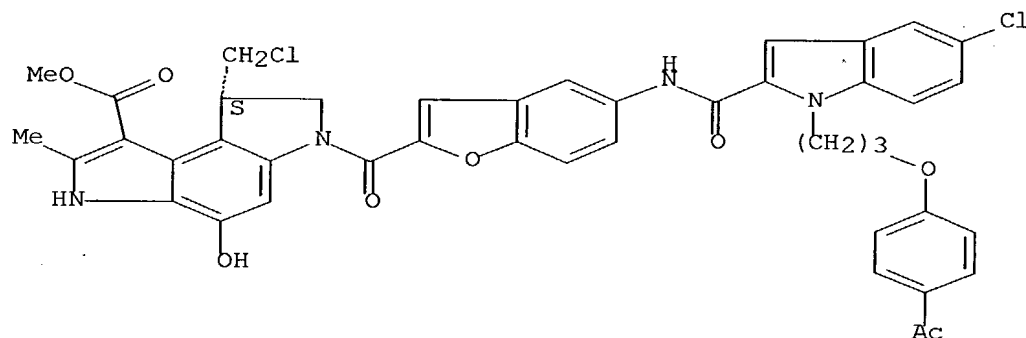
Absolute stereochemistry.



RN 477208-66-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[1-[3-(4-acetylphenoxy)propyl]-5-chloro-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

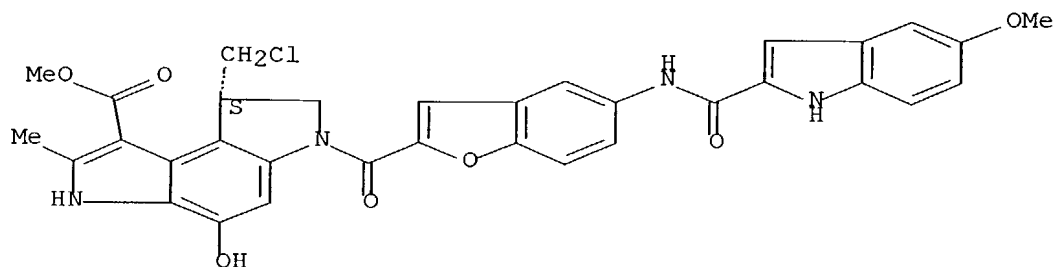
Absolute stereochemistry.



RN 477208-67-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[[5-[[5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

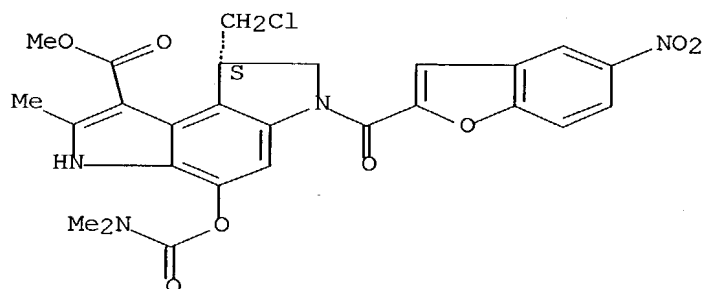
Absolute stereochemistry.



RN 477208-69-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-
2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

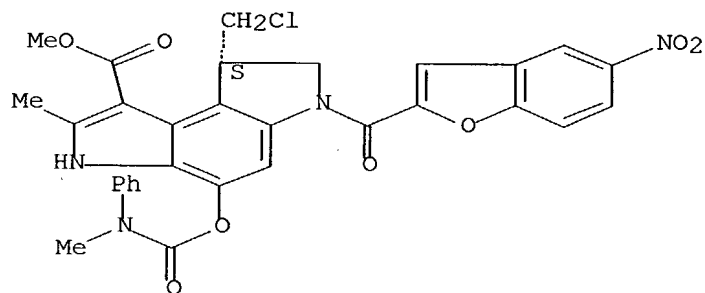
Absolute stereochemistry.



RN 477208-70-1 CAPLUS

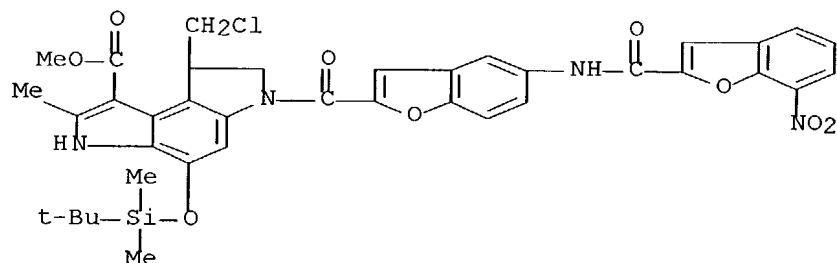
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-2-methyl-4-[(methylphenylamino)carbonyl]oxy]-6-[(5-nitro-2-
benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



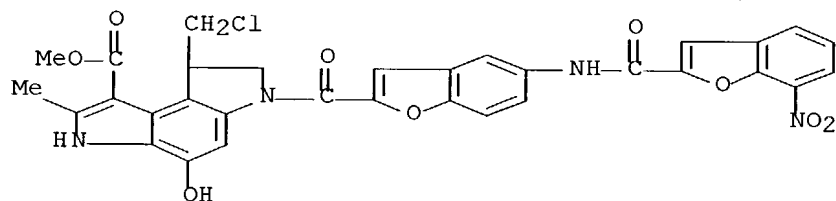
RN 477208-71-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[(7-
nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl
ester (9CI) (CA INDEX NAME)



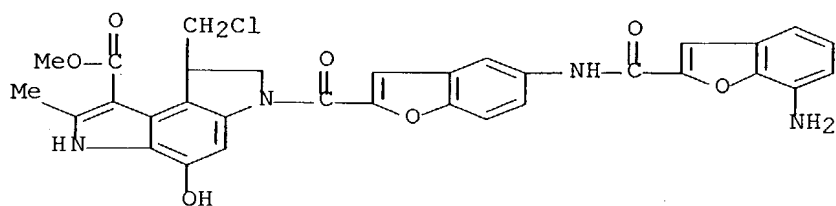
RN 477208-72-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-methyl-6-[[5-[[(7-nitro-2-
benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester
(9CI)
(CA INDEX NAME)



RN 477208-73-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(7-amino-2-
benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester (9CI) (CA INDEX
NAME)

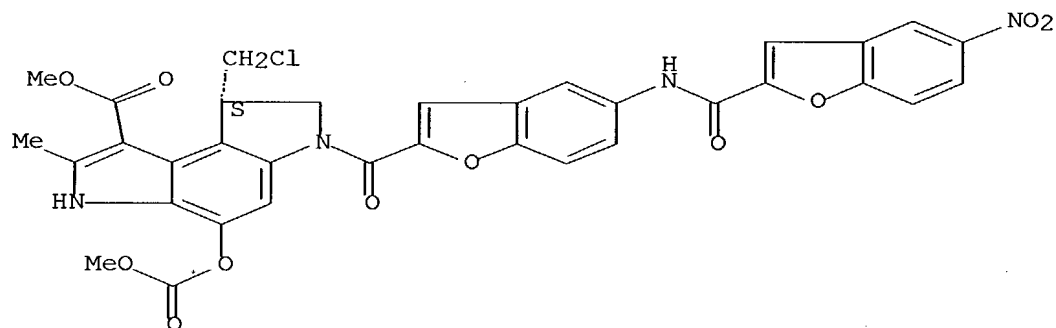


RN 477208-75-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(methoxycarbonyl)oxy]-6-[[5-[[[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

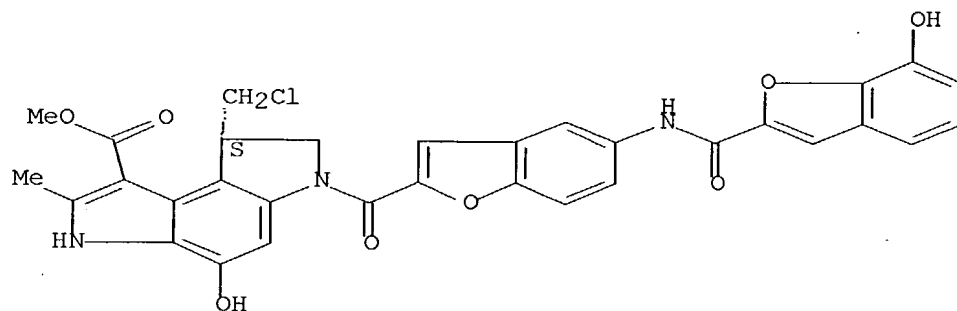


RN 477208-77-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-6-[[5-[[[(7-hydroxy-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477208-78-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[[1-[3-[4-[18-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-methyl-4-oxo-7,10,13,16-tetraoxa-2,3-diazaoctadec-1-en-1-yl]phenoxy]propyl]-5-methoxy-

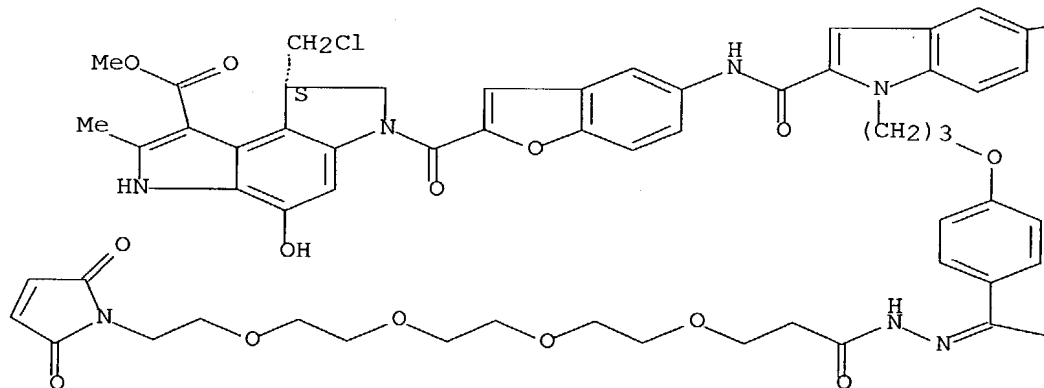
1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-

4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

PAGE 1-A



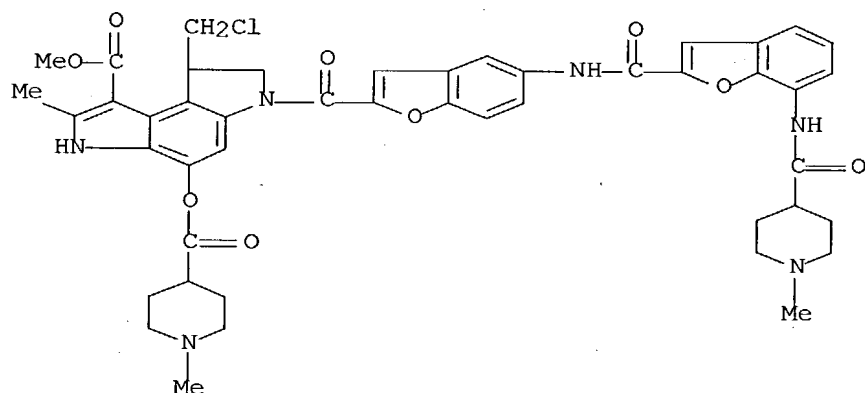
—OMe

—Me

RN 477208-79-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

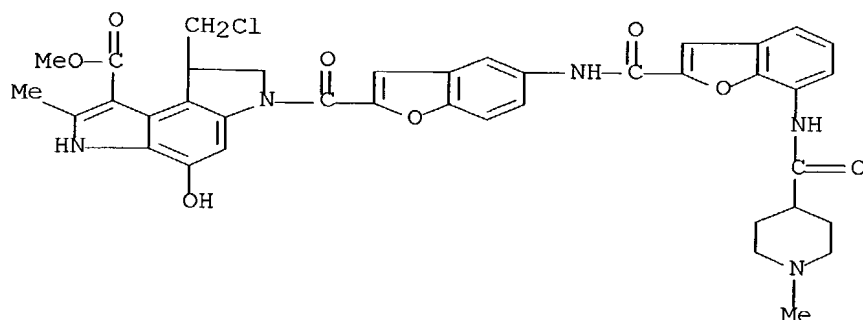
tetrahydro-2-methyl-6-[[5-[[[7-[[1-methyl-4-piperidinyl)carbonyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-4-[[1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 477208-80-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-methyl-6-[[5-[[[7-[[1-methyl-4-piperidinyl)carbonyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

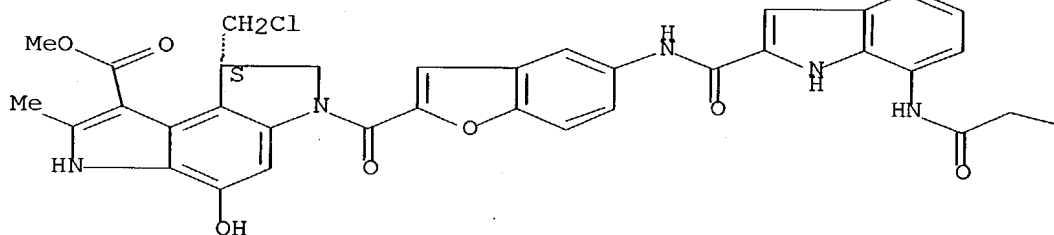


RN 477208-81-4 CAPLUS

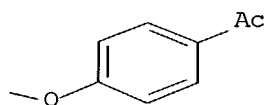
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[(4-acetylphenoxy)acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 477208-82-5 CAPLUS

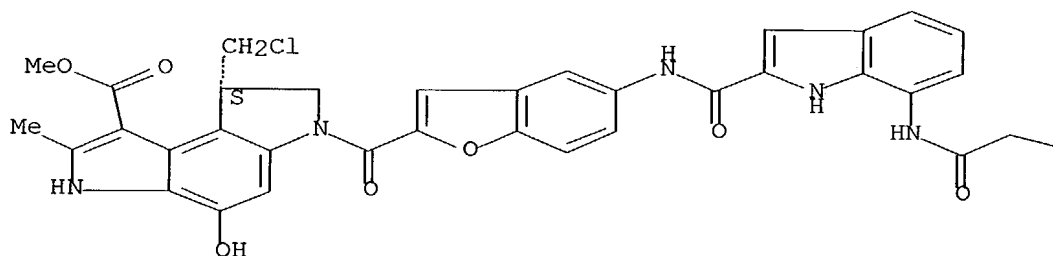
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[[7-[[[4-[24-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-methyl-4-oxo-7,10,13,16,19,22-hexaoxa-2,3-diazatetracos-1-en-1-yl]phenoxy]acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-

4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

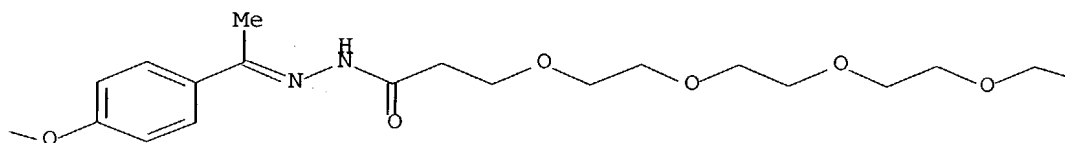
Absolute stereochemistry.

Double bond geometry unknown.

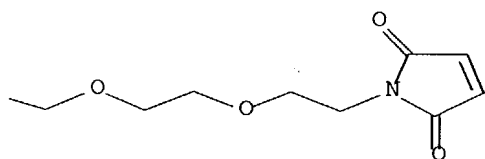
PAGE 1-A



PAGE 1-B



PAGE 1-C

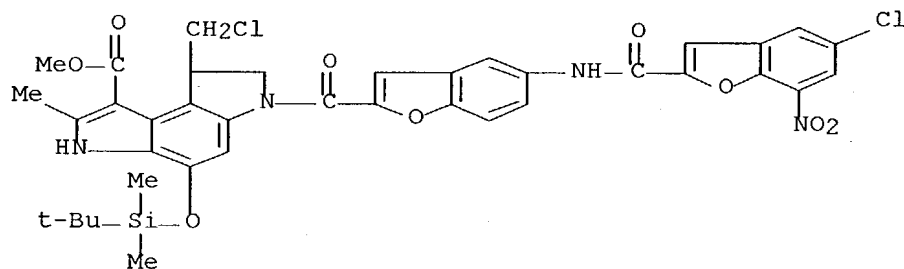


RN 477208-83-6 CAPLUS

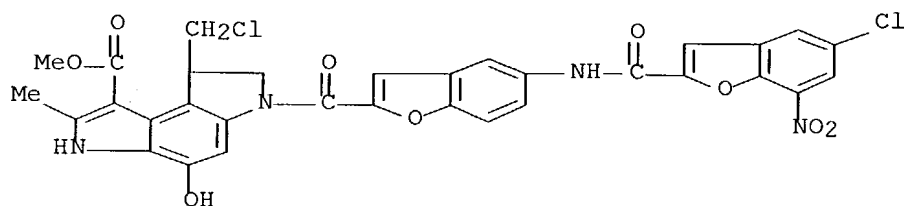
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[[7-[2-[2-(2-ethoxyethoxy)ethoxy]ethoxy]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
[[5-chloro-7-nitro-2-benzofuranyl)carbonyl]amino]-2-
benzofuranyl)carbonyl]-4-[[1,1-dimethylethyl)dimethylsilyl]oxy]-
3,6,7,8-
tetrahydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

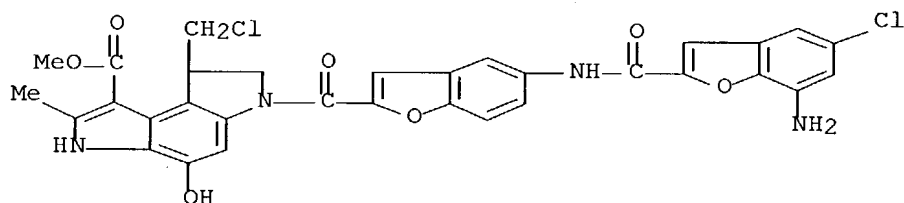


CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
[[(5-chloro-7-nitro-2-benzofuranyl) carbonyl] amino]-2-
benzofuranyl] carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl
ester (9CI) (CA INDEX NAME)



RN 477208-86-9 CAPLUS

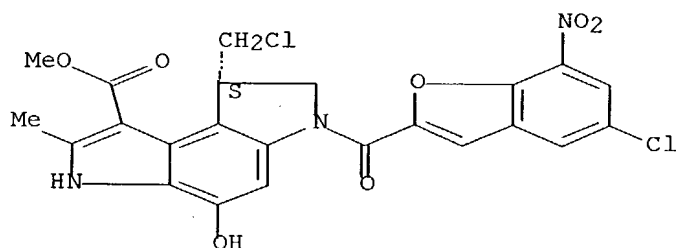
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[7-amino-5-chloro-2-benzofuranyl) carbonyl] amino]-2-benzofuranyl] carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 477208-87-0 CAPLUS

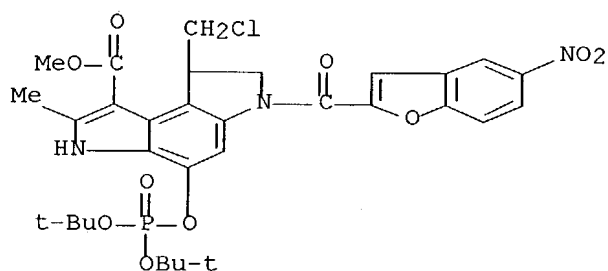
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[(5-chloro-7-nitro-2-benzofuranyl) carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477208-88-1 CAPLUS

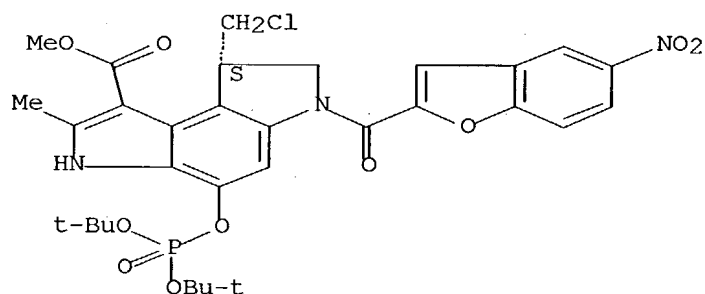
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[bis(1,1-dimethylethoxy)phosphinyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl) carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 477208-89-2 CAPLUS

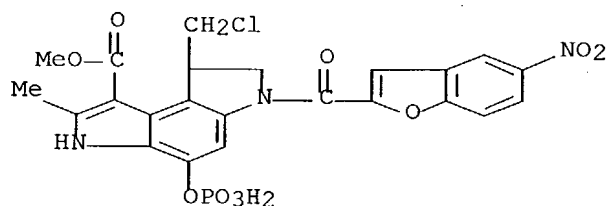
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[bis(1,1-dimethylethoxy)phosphinyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



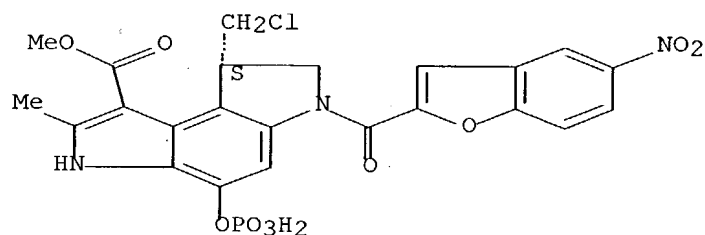
RN 477208-90-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-4-(phosphonooxy)-, 1-methyl ester (9CI) (CA INDEX NAME)



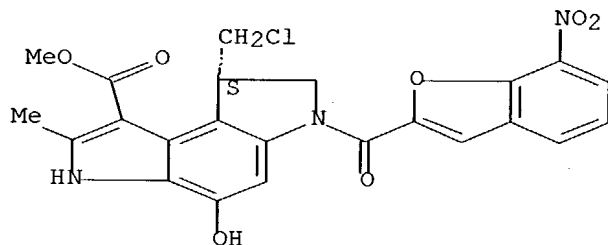
RN 477208-91-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-4-
 (phosphonooxy)-
 , 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



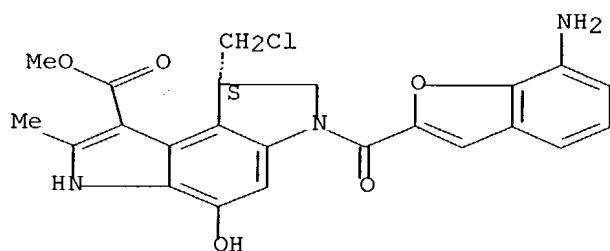
RN 477208-92-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-methyl-6-[(7-nitro-2-benzofuranyl)carbonyl]-,
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477208-93-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(7-amino-2-
 benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-
 methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

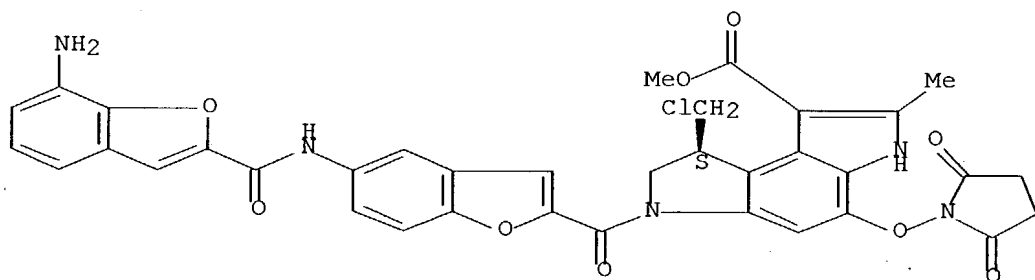
Absolute stereochemistry.



RN 477208-94-9 CAPLUS

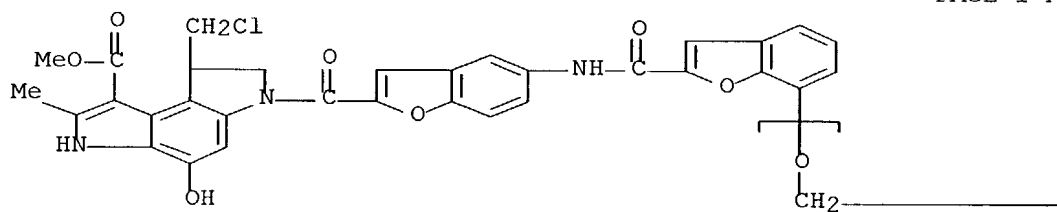
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(7-amino-2-benzofuranyl) carbonyl] amino]-2-benzofuranyl] carbonyl]-8-(chloromethyl)-4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

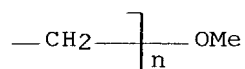


RN 477208-95-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl] carbonyl]-5-benzofuranyl] amino] carbonyl]-7-benzofuranyl]- ω -methoxy- (9CI) (CA INDEX NAME)



PAGE 1-A

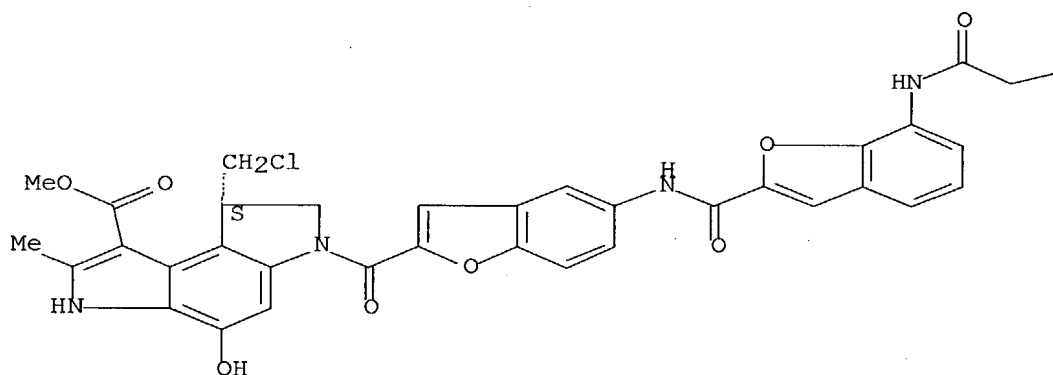


RN 477208-96-1 CAPLUS

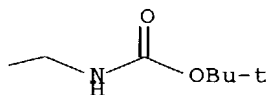
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[[7-[[3-[[1,1-dimethylethoxy)carbonyl]amino]-1-oxopropyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



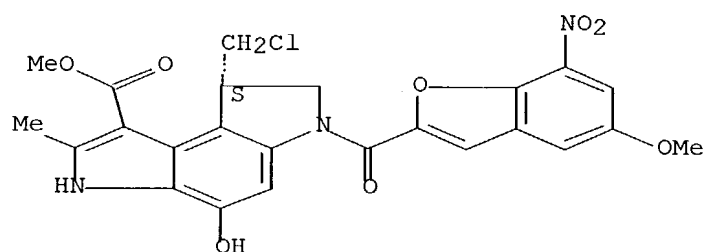
PAGE 1-B



RN 477208-97-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(5-methoxy-7-nitro-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

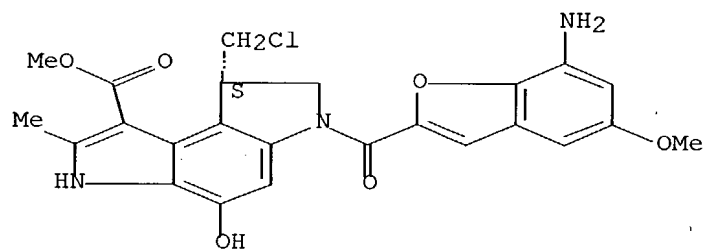
Absolute stereochemistry.



RN 477208-98-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(7-amino-5-methoxy-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

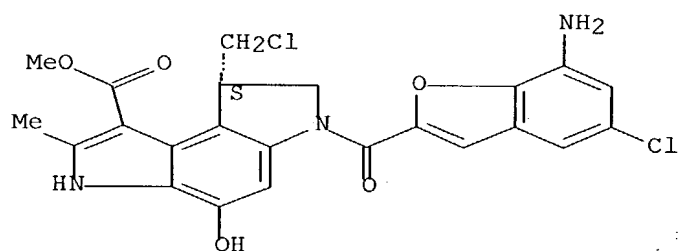
Absolute stereochemistry.



RN 477208-99-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(7-amino-5-chloro-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-00-0 CAPLUS

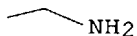
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[(3-amino-1-oxopropyl)amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl

benzofuranyl]carbonyl]-8-
(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester,
(8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

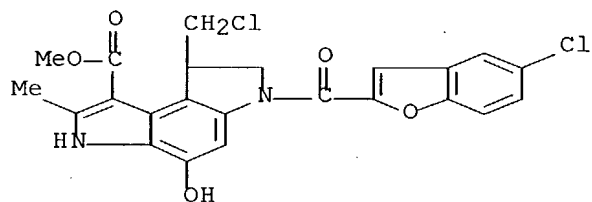


PAGE 1-B



RN 477209-01-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-chloro-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

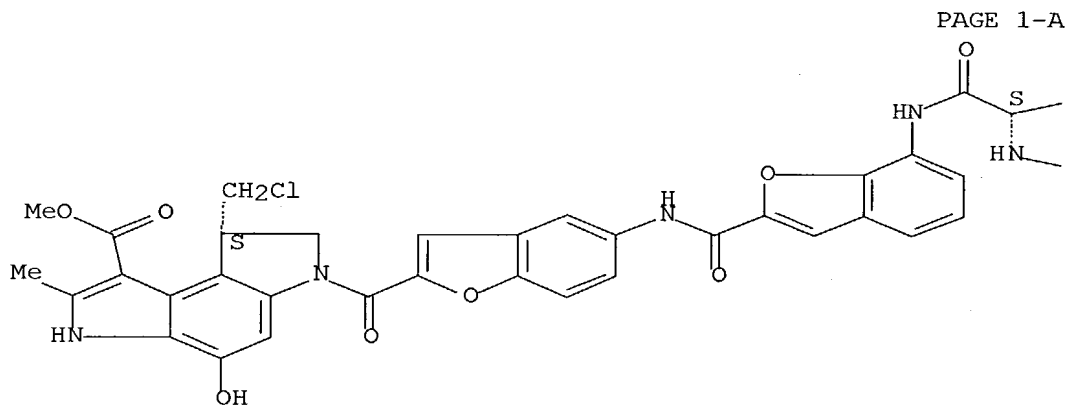


RN 477209-02-2 CAPLUS

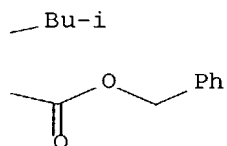
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-hydroxy-2-methyl-6-[[5-[[[7-[[(2S)-4-methyl-1-oxo-2-
 [[(phenylmethoxy) carbonyl] amino] pentyl] amino]-2-
 benzofuranyl] carbonyl] amino]-2-benzofuranyl] carbonyl]-, methyl ester,
 (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

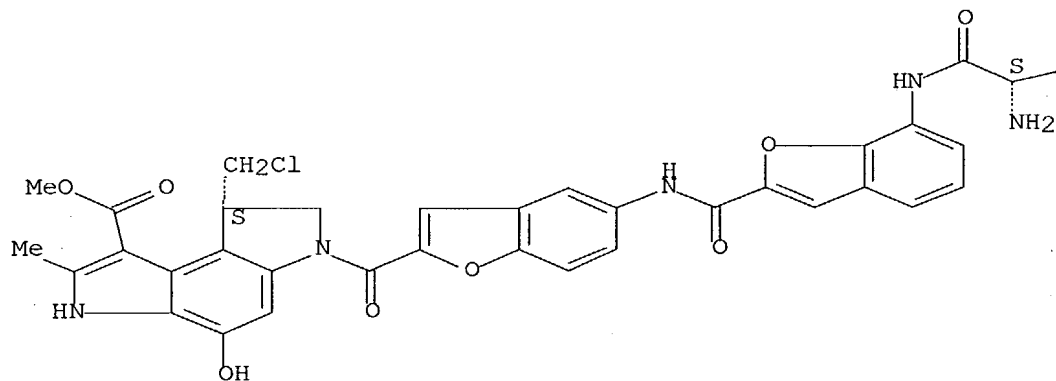


PAGE 1-B



RN 477209-03-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[(2S)-2-
 amino-
 4-methyl-1-oxopentyl] amino]-2-benzofuranyl] carbonyl] amino]-2-
 benzofuranyl] carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-
 methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

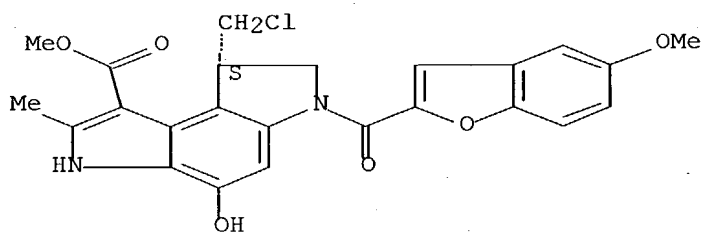
Absolute stereochemistry.



—Bu-i

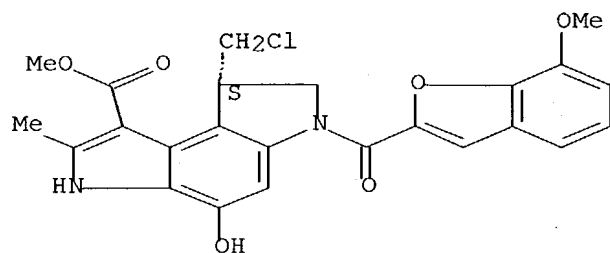
RN 477209-04-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-,
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-05-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(7-methoxy-2-benzofuranyl)carbonyl]-2-methyl-,
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

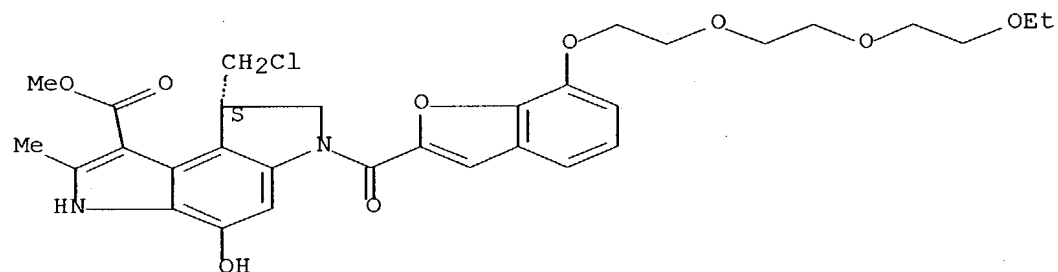
Absolute stereochemistry.



RN 477209-06-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[7-[2-[2-(2-ethoxyethoxy)ethoxy]ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

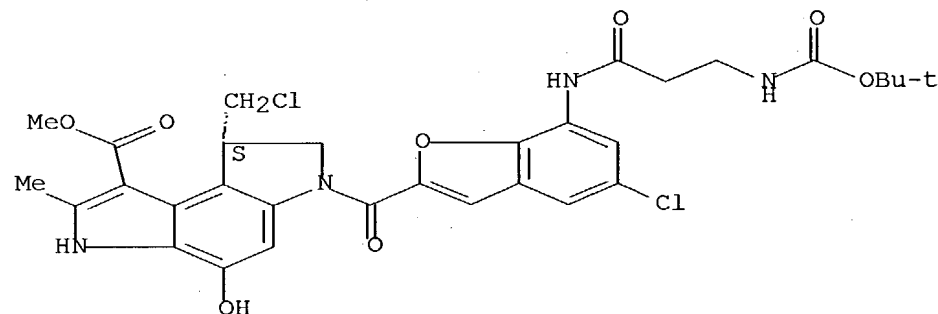
Absolute stereochemistry.



RN 477209-07-7 CAPLUS

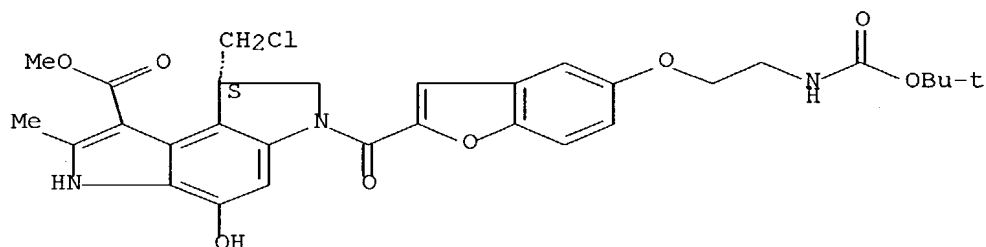
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-chloro-7-[[3-[[1,1-dimethylethoxy)carbonyl]amino]-1-oxopropyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



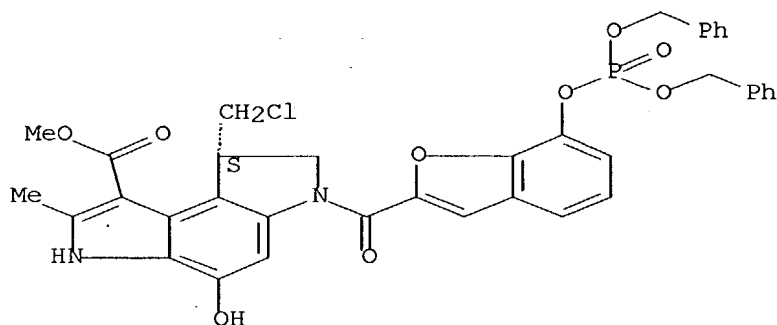
RN 477209-08-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
 [2-
 [[(1,1-dimethylethoxy)carbonyl]amino]ethoxy]-2-benzofuranyl]carbonyl]-
 3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



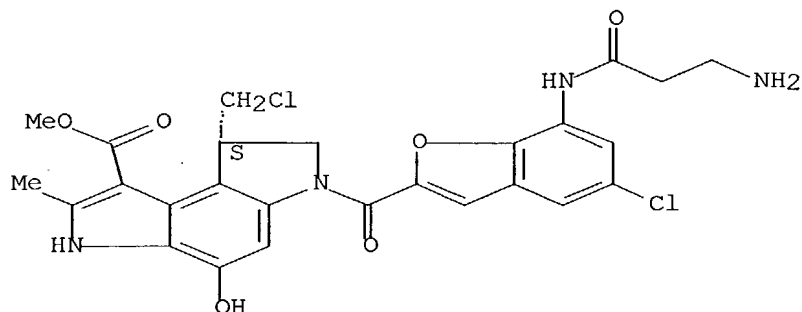
RN 477209-09-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[7-
 [[bis(phenylmethoxy)phosphinyl]oxy]-2-benzofuranyl]carbonyl]-8-
 (chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester,
 (8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-10-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[7-[(3-amino-1-
 oxopropyl)amino]-5-chloro-2-benzofuranyl]carbonyl]-8-(chloromethyl)-
 3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA
 INDEX NAME)

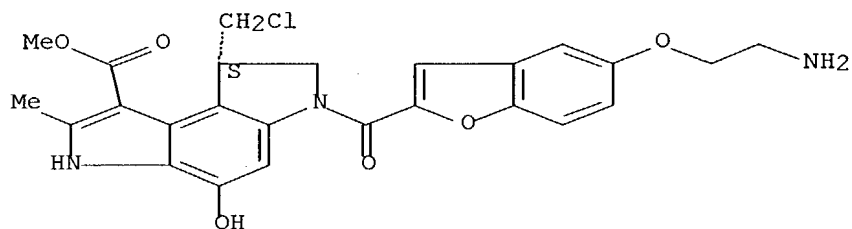
Absolute stereochemistry.



RN 477209-11-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-(2-aminoethoxy)-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

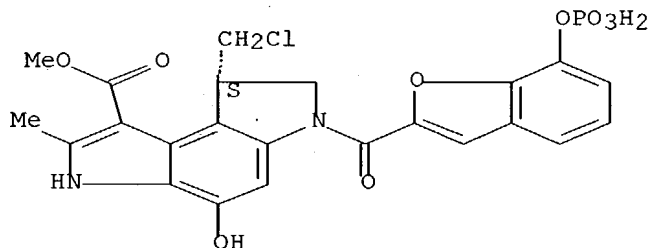
Absolute stereochemistry.



RN 477209-12-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[[7-(phosphonoxy)-2-benzofuranyl]carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

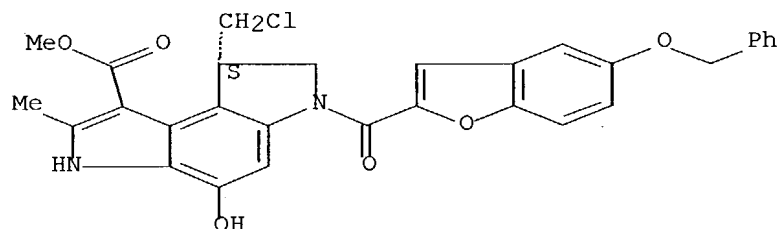
Absolute stereochemistry.



RN 477209-14-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-methyl-6-[[5-(phenylmethoxy)-2-
benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

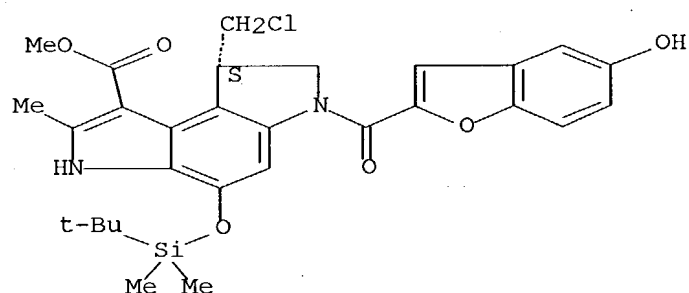
Absolute stereochemistry.



RN 477209-15-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[(5-hydroxy-2-
benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

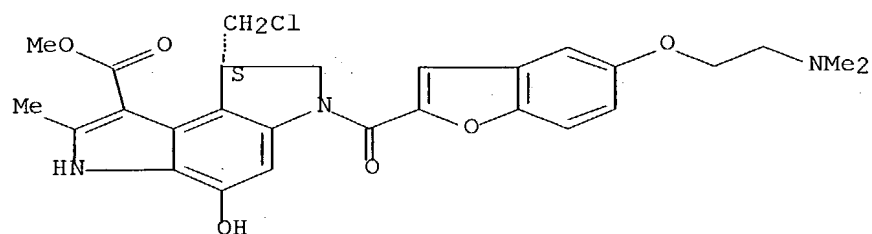
Absolute stereochemistry.



RN 477209-16-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
[2-
(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-
hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

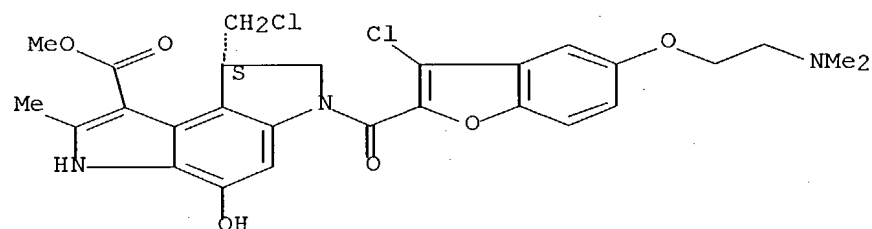
Absolute stereochemistry.



RN 477209-17-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[3-chloro-5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

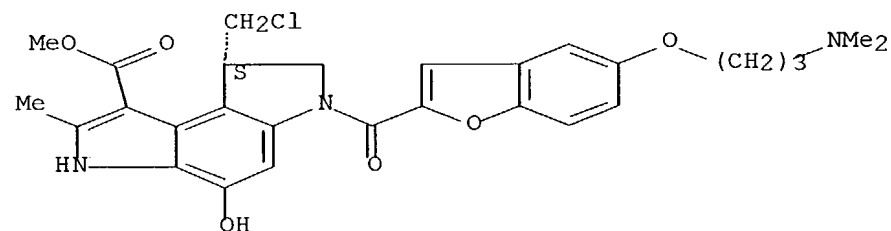
Absolute stereochemistry.



RN 477209-18-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[3-(dimethylamino)propoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



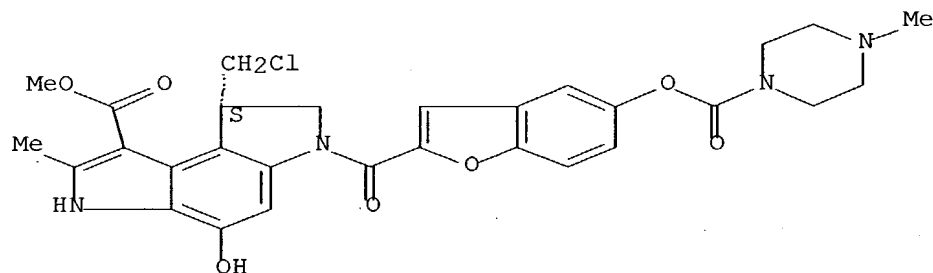
RN 477209-19-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-

3,6,7,8-

tetrahydro-4-hydroxy-2-methyl-6-[[5-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

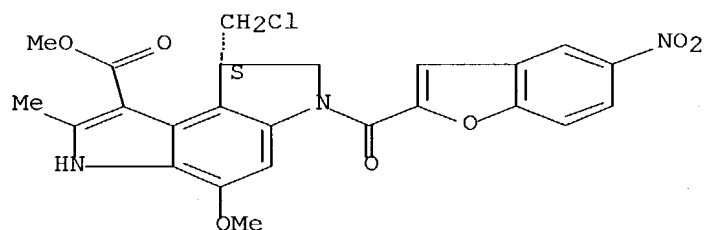


RN 477209-20-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-methoxy-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

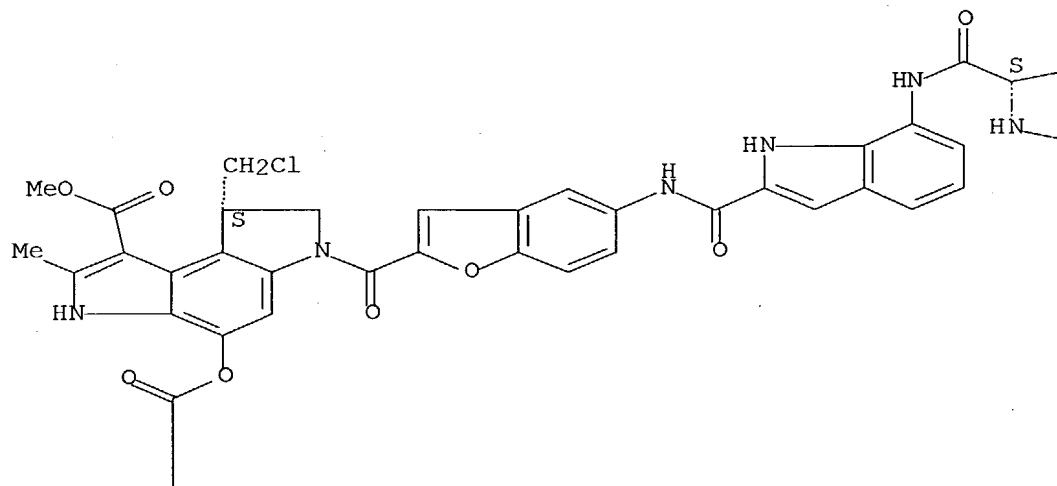


RN 477209-21-5 CAPLUS

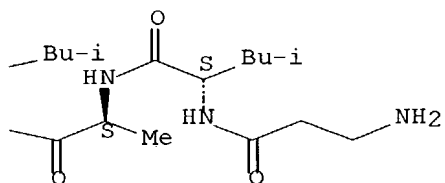
CN L-Leucinamide, β -alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[1S]-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

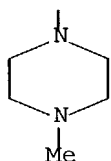
PAGE 1-A



PAGE 1-B



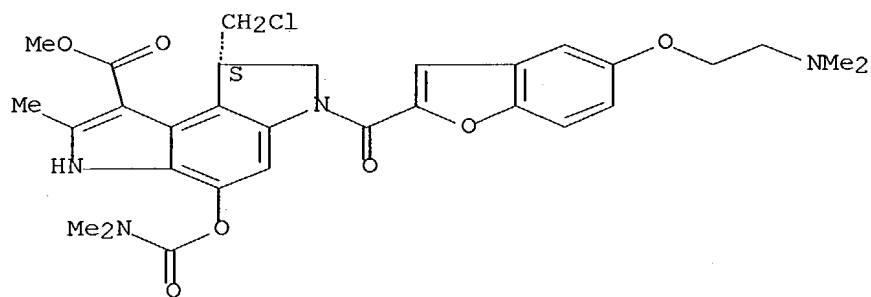
PAGE 2-A



RN 477209-23-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[(dimethylamino) carbonyl]oxy]-6-[[5-[2-(dimethylamino)ethoxy]-2-
benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-
(9CI) (CA INDEX NAME)

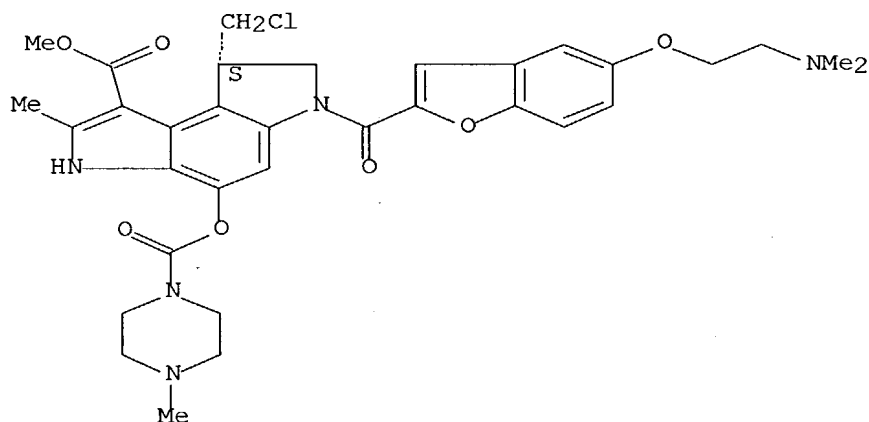
Absolute stereochemistry.



RN 477209-24-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

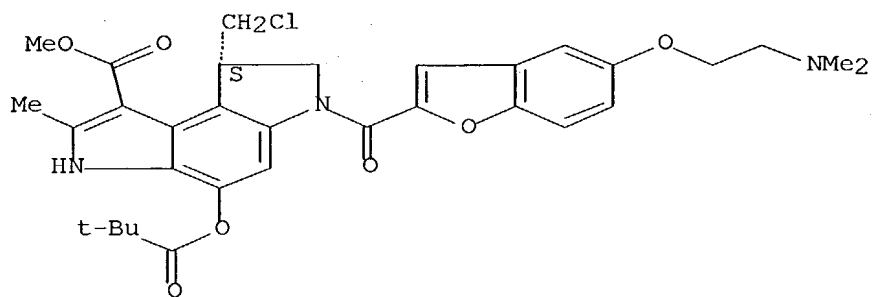
Absolute stereochemistry.



RN 477209-25-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-(2,2-dimethyl-1-oxopropoxy)-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

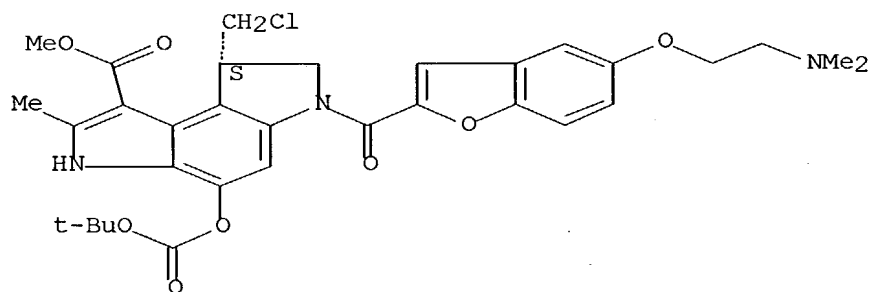
Absolute stereochemistry.



RN 477209-26-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[1,1-dimethylethoxy)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

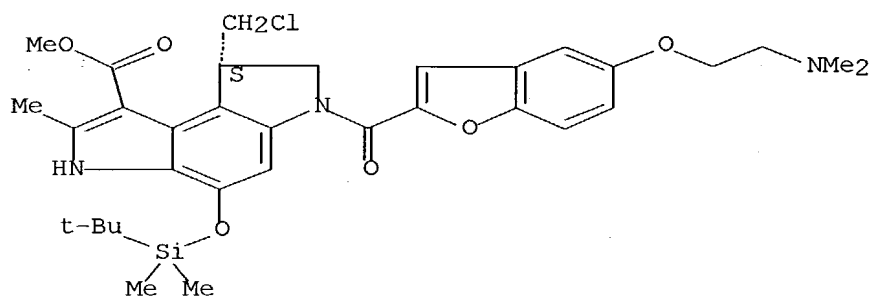
Absolute stereochemistry.



RN 477209-27-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

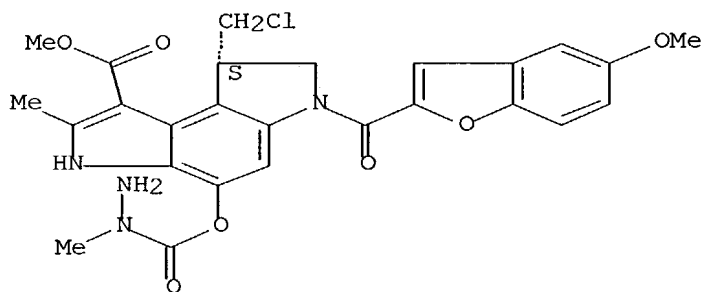


RN 477209-28-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[[1-methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

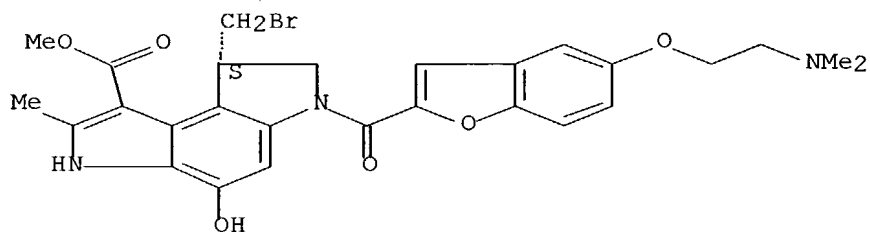


RN 477209-29-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[[5-[2-

(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

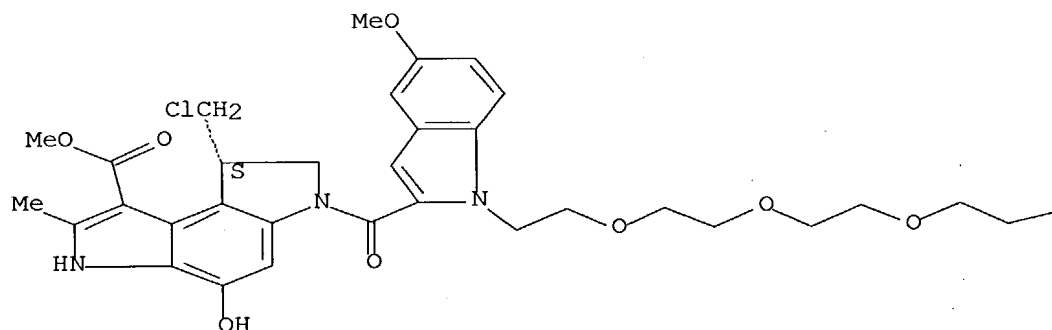
Absolute stereochemistry.



RN 477209-30-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-methoxy-1-(3,6,9,12-tetraoxatridec-1-yl)-1H-
 indol-2-yl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

PAGE 1-A

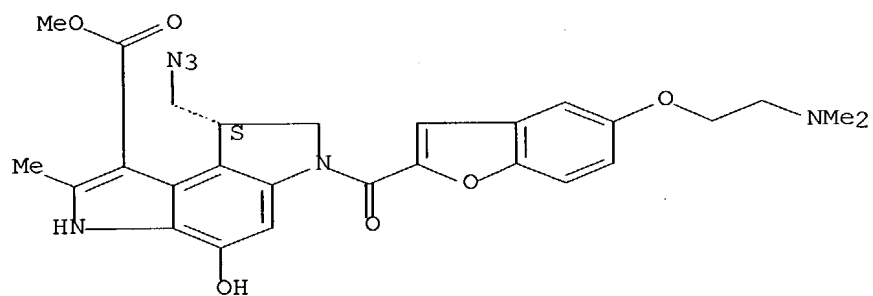


PAGE 1-B

—OMe

RN 477209-31-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(azidomethyl)-6-[[5-
 [2-
 (dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-
 hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

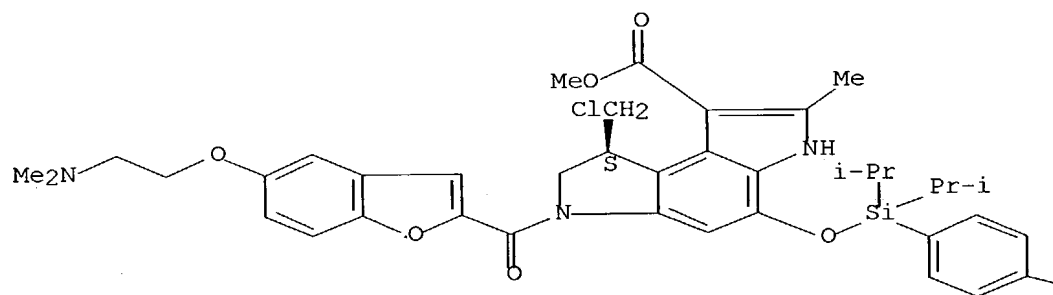
Absolute stereochemistry.



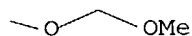
RN 477209-32-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[[4-(methoxymethoxy)phenyl]bis(1-methylethyl)silyl]oxy]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

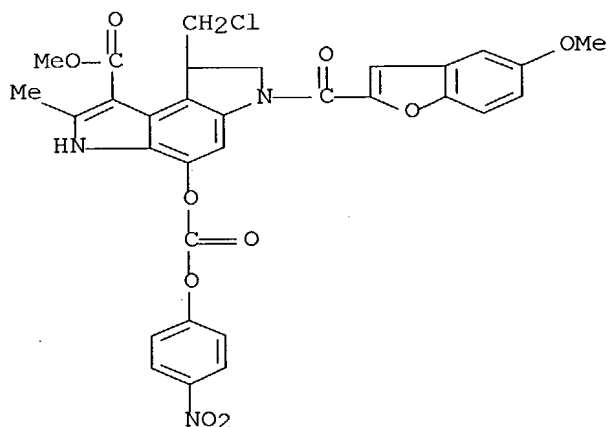


PAGE 1-B



RN 477209-33-9 CAPLUS

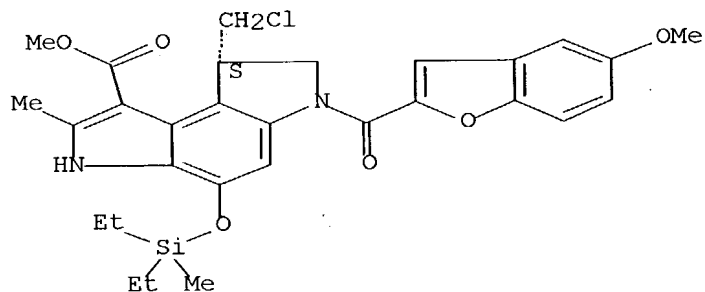
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[[4-nitrophenoxy)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 477209-34-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[(diethylmethylsilyl)oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

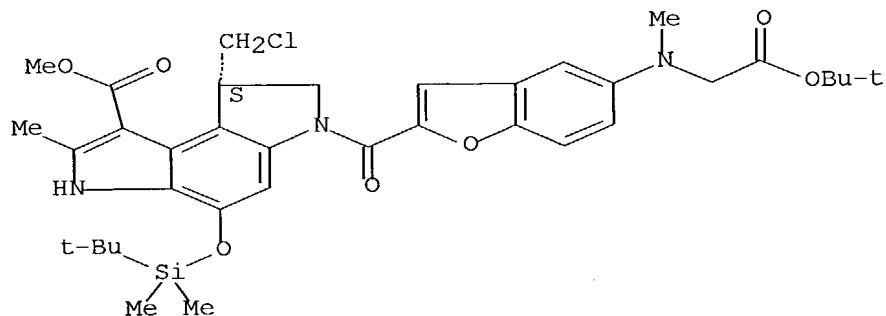
Absolute stereochemistry.



RN 477209-35-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[(1,1-dimethylethoxy)-2-oxoethyl]methylamino]-2-benzofuranyl]carbonyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

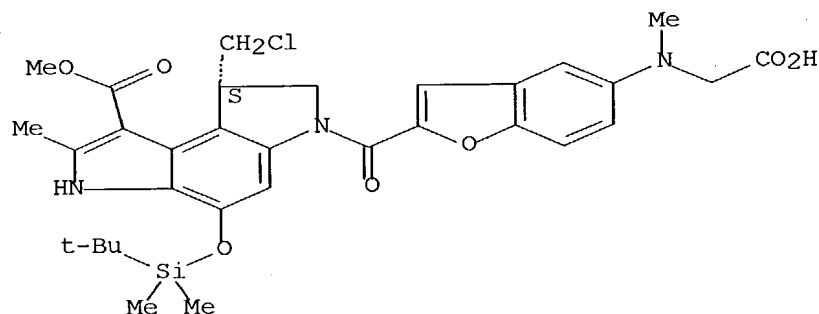
Absolute stereochemistry.



RN 477209-36-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-
 4- [[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,
 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

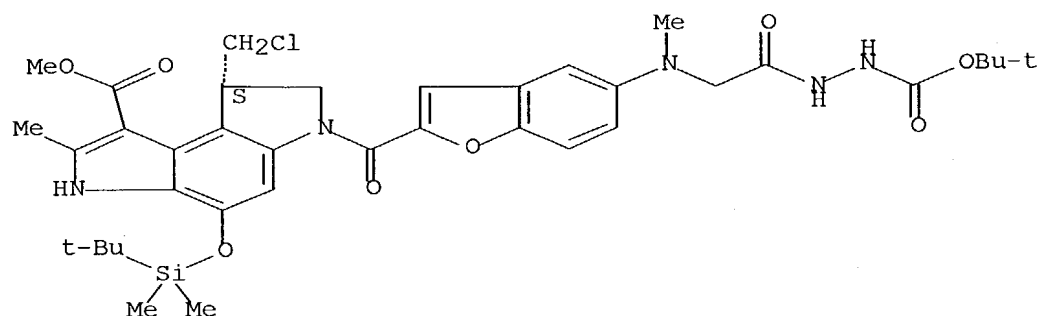
Absolute stereochemistry.



RN 477209-37-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
 [[2-
 [2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-oxoethyl]methylamino]-2-
 benzofuran]carbonyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-
 3,6,7,8-
 tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

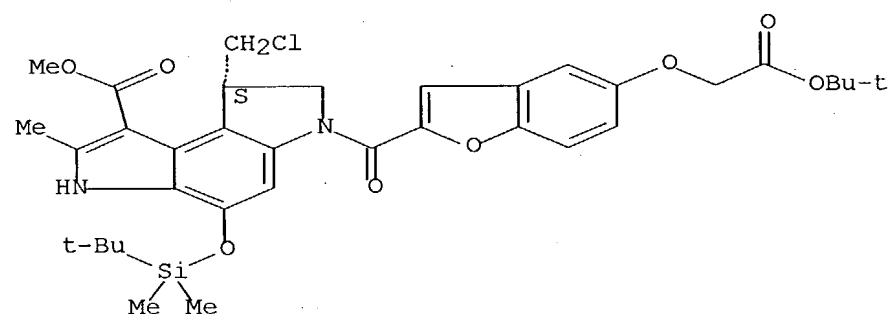
Absolute stereochemistry.



RN 477209-38-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
[2-
[(1,1-dimethylethoxy)carbonyl]-2-oxoethoxy]-2-benzofuranyl]carbonyl]-4-
[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

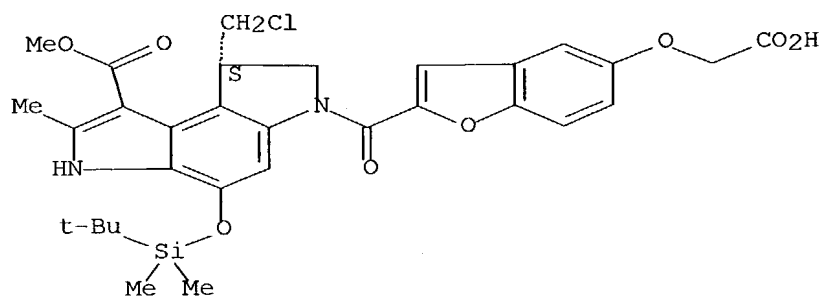
Absolute stereochemistry.



RN 477209-39-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-(carboxymethoxy)-
2-
benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

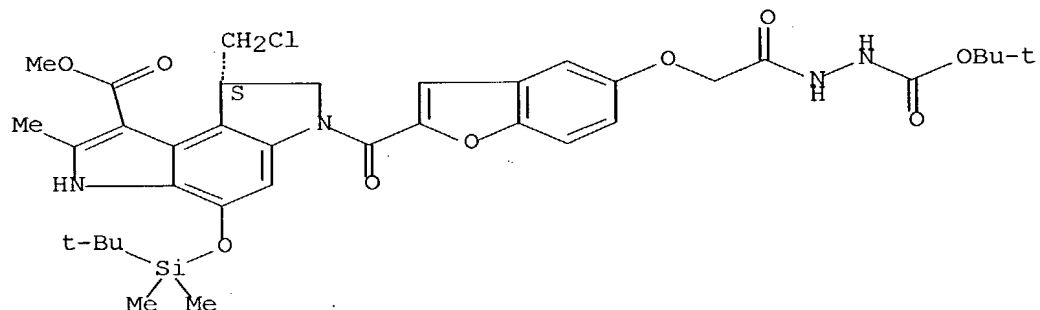
Absolute stereochemistry.



RN 477209-40-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-
[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-oxoethoxy]-2-
benzofuranyl]carbonyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-
3,6,7,8-
tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

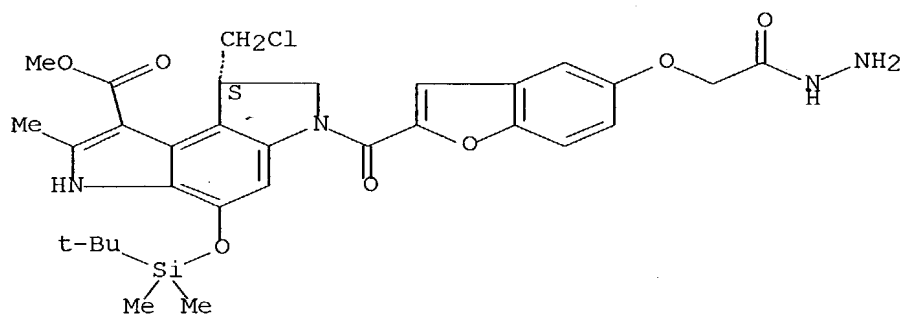
Absolute stereochemistry.



RN 477209-41-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-6-[[5-(2-hydrazino-2-oxoethoxy)-2-
benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-
(9CI) (CA INDEX NAME)

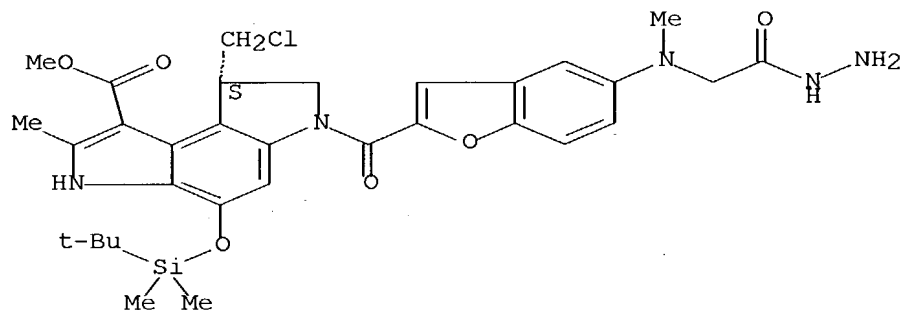
Absolute stereochemistry.



RN 477209-42-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-[(2-hydrazino-2-oxoethyl)methylamino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-
 , methyl ester, (8S)- (9CI) (CA INDEX NAME)

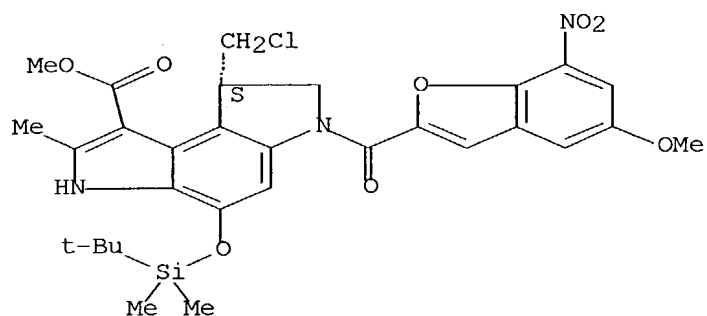
Absolute stereochemistry.



RN 477209-43-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-7-nitro-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

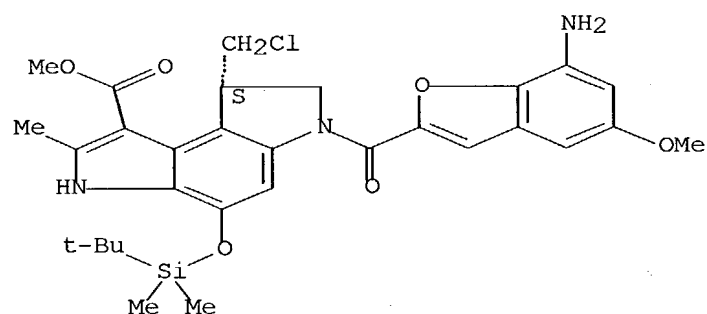
Absolute stereochemistry.



RN 477209-44-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(7-amino-5-methoxy-2-benzofuranyl)carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

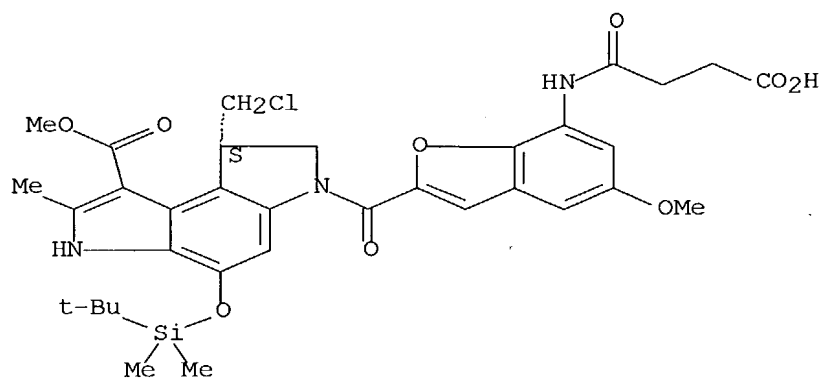
Absolute stereochemistry.



RN 477209-45-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[7-[(3-carboxy-1-oxopropoxy)amino]-5-methoxy-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

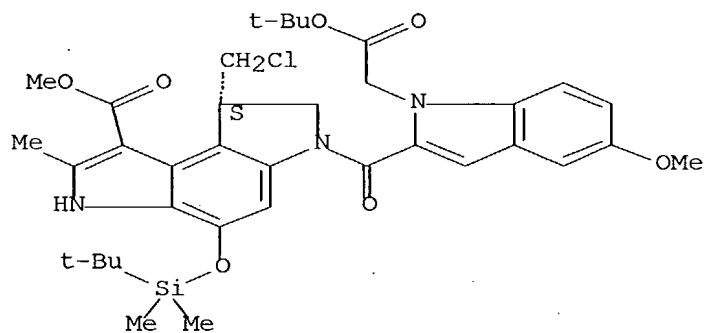


RN 477209-47-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[1-

[2-(1,1-dimethylethoxy)-2-oxoethyl]-5-methoxy-1H-indol-2-yl]carbonyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

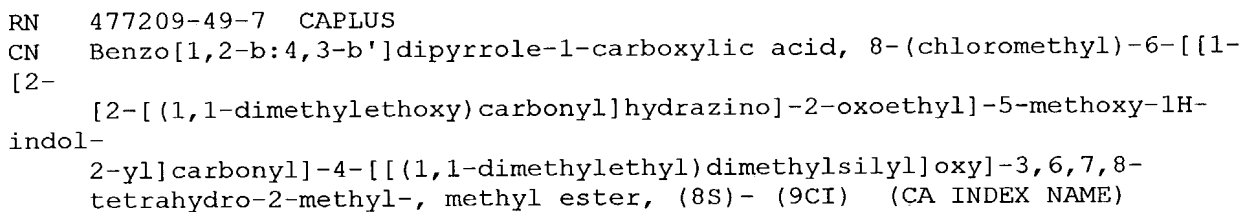
Absolute stereochemistry.



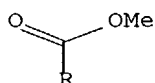
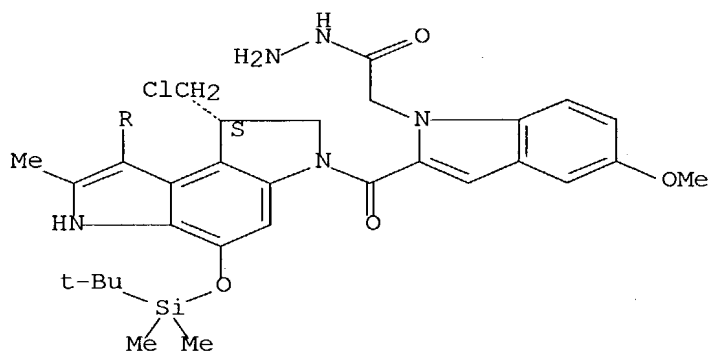
RN 477209-48-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[1-(carboxymethyl)-5-methoxy-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

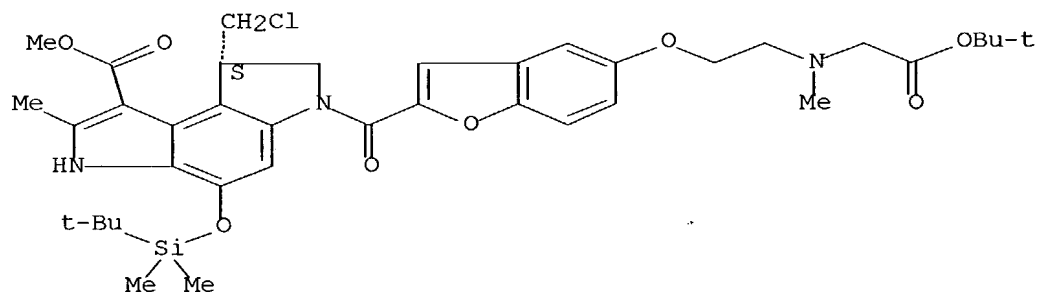
COC(=O)c1c[nH]c2c(c1)c(O[Si](C)(C)C(C)(C)C)c(OCCN(C)C(=O)c3c[nH]c4cc(OC)ccc43)cc2Cl

Absolute stereochemistry.



RN 477209-51-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-[[2-(1,1-dimethylethoxy)-2-oxoethyl]methylamino]ethoxy]-2-benzofuranyl]carbonyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

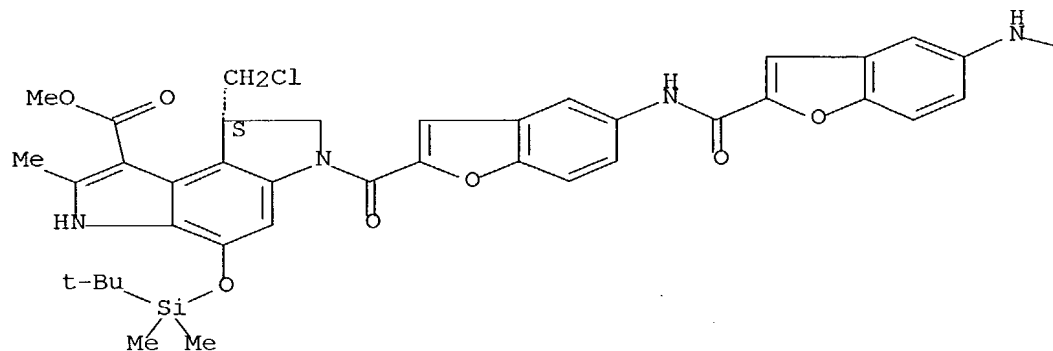
Absolute stereochemistry.



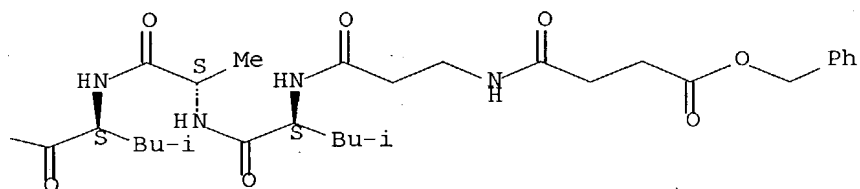
RN 477209-52-2 CAPLUS
 CN L-Leucinamide, N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



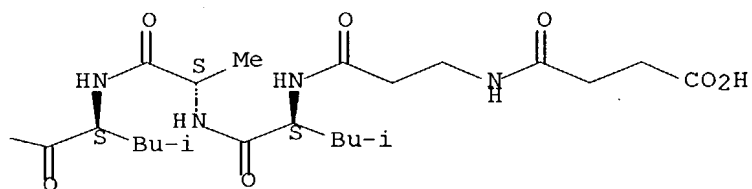
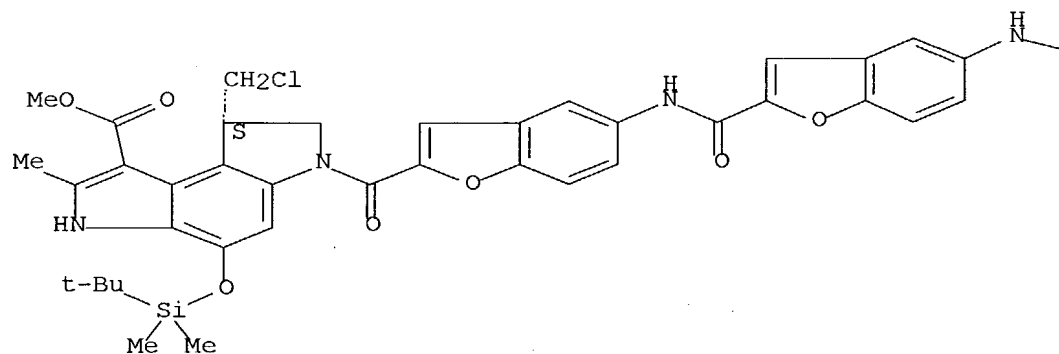
PAGE 1-B



RN 477209-54-4 CAPLUS

CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

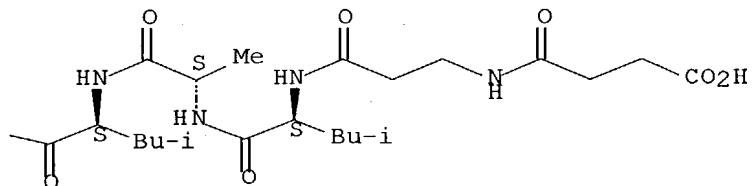
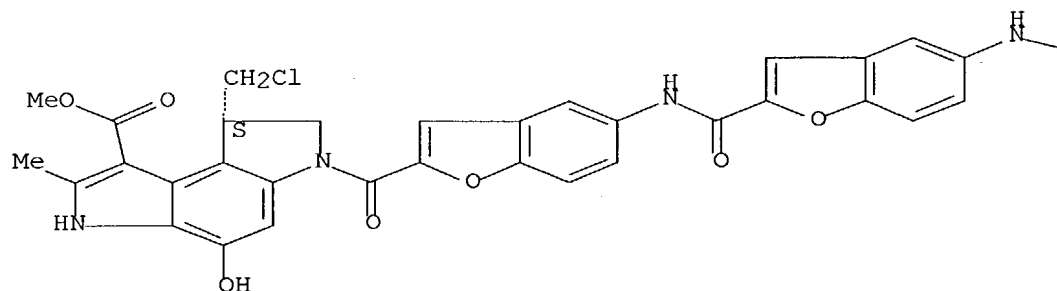
Absolute stereochemistry.



RN 477209-56-6 CAPLUS

CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

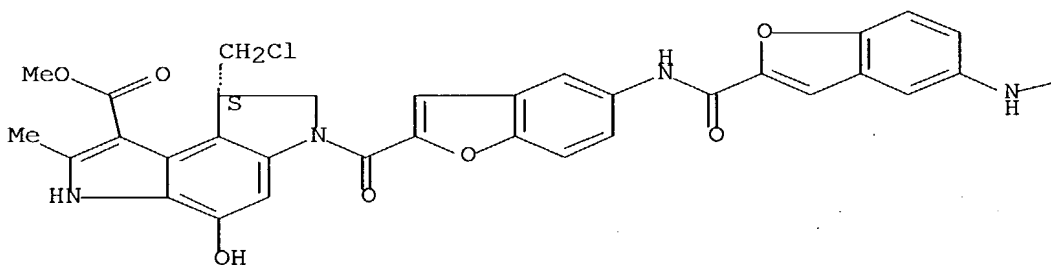
Absolute stereochemistry.

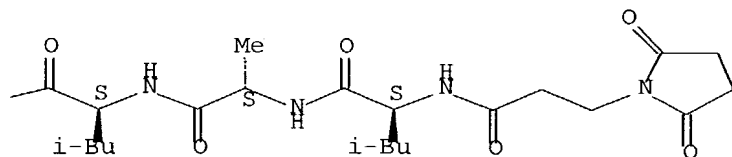


RN 477209-57-7 CAPLUS

CN L-Leucinamide, N-[3-(2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

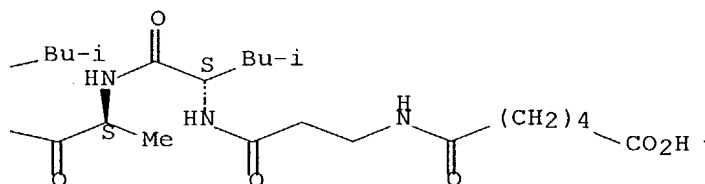
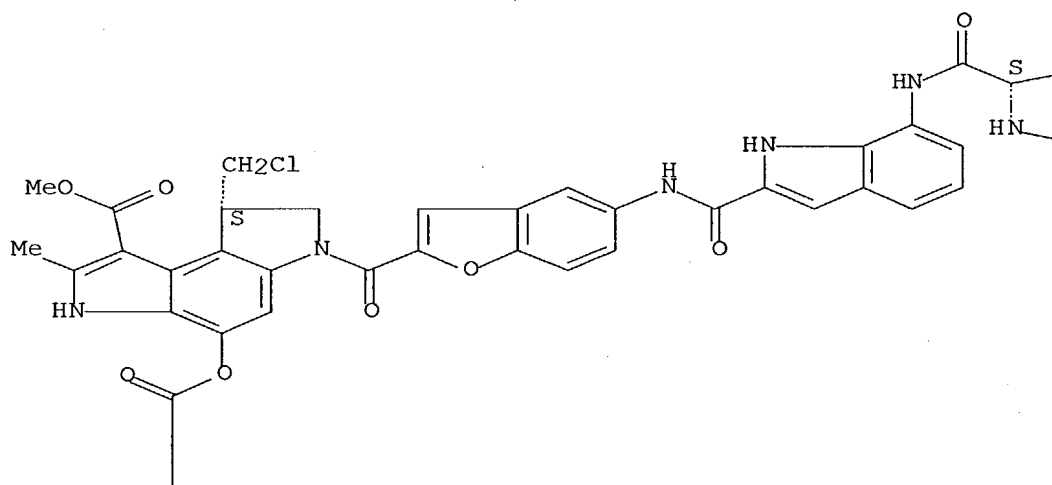


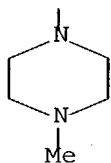


RN 477209-59-9 CAPLUS

CN L-Leucinamide, N-(5-carboxy-1-oxopentyl)- β -alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[1S]-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

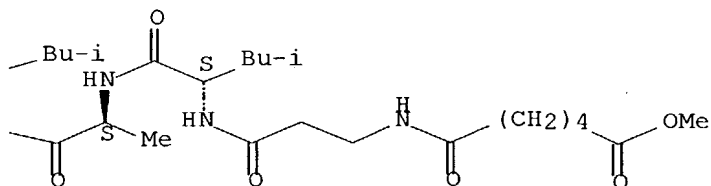
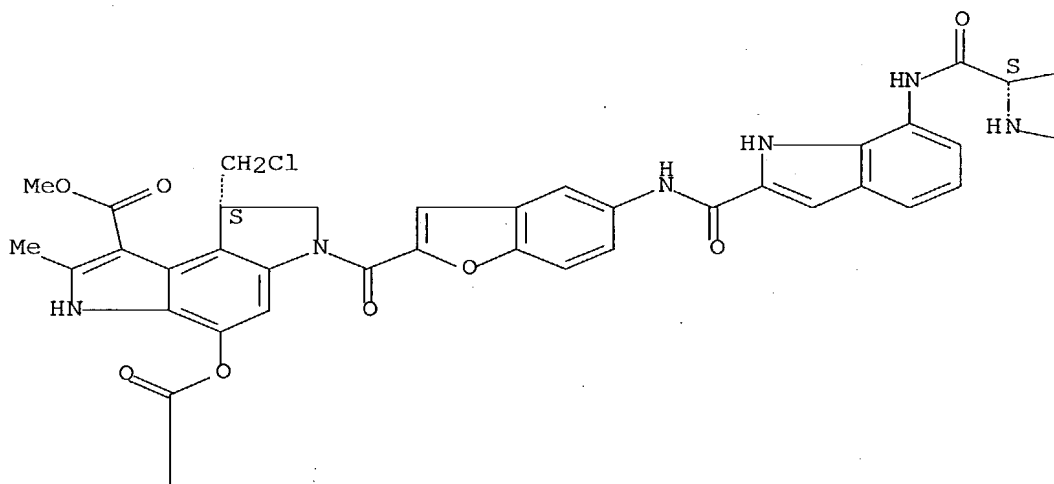


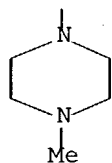


RN 477209-60-2 CAPLUS

CN L-Leucinamide, N-(6-methoxy-1,6-dioxohexyl)- β -alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





RN 477209-61-3 CAPLUS

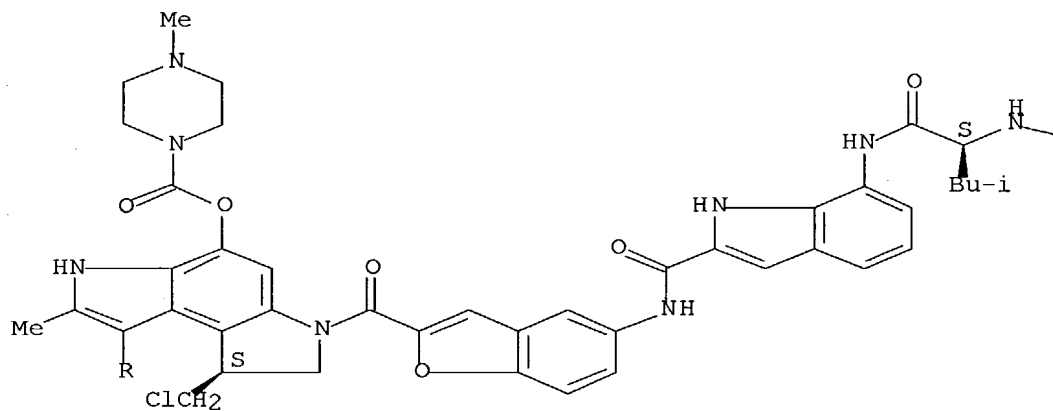
CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-

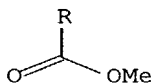
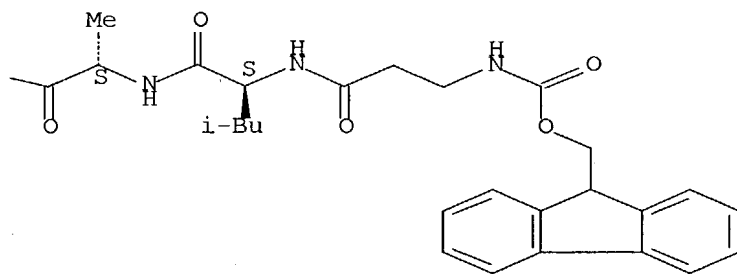
(methoxycarbonyl)-

7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-

7-yl]-dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





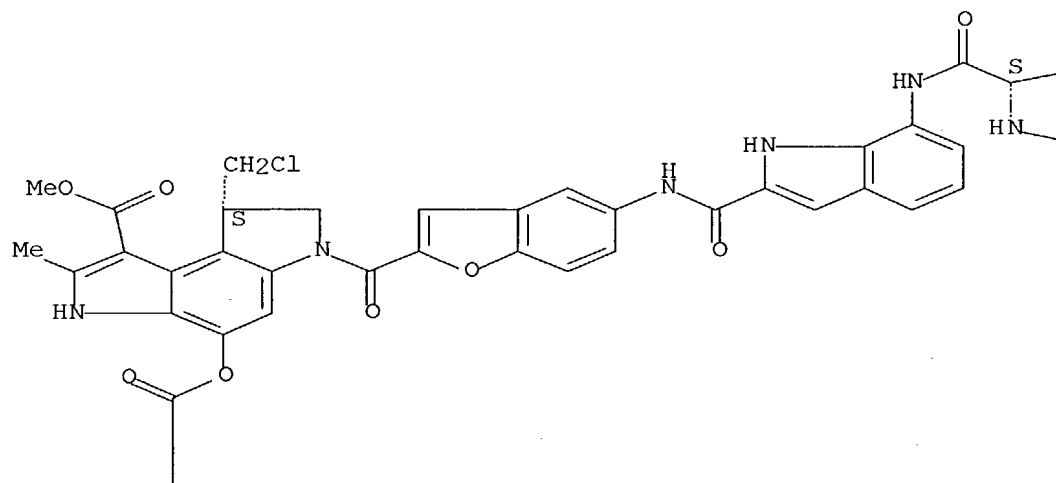
RN 477209-62-4 CAPLUS

CN L-Leucinamide, N-[1,6-dioxo-6-(phenylmethoxy)hexyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-

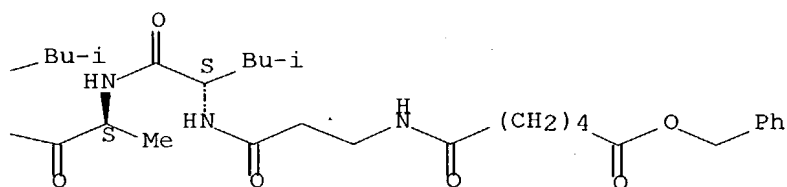
7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

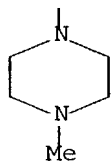
PAGE 1-A



PAGE 1-B



PAGE 2-A



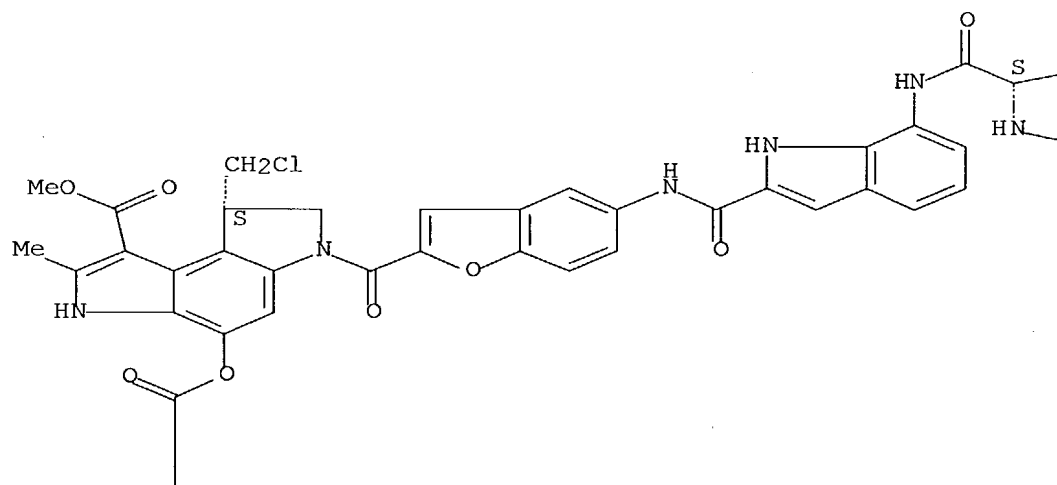
RN 477209-63-5 CAPLUS

CN L-Leucinamide, N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[1-(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-

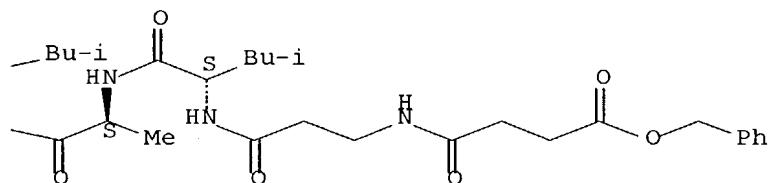
7-methyl-5-[[4-methyl-1-piperazinyl]carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

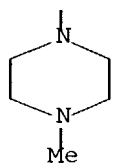
PAGE 1-A



PAGE 1-B



PAGE 2-A

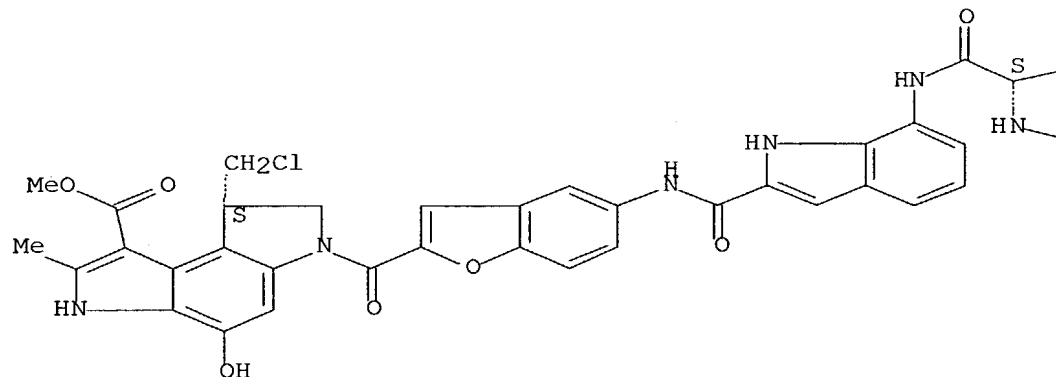


RN 477209-64-6 CAPLUS

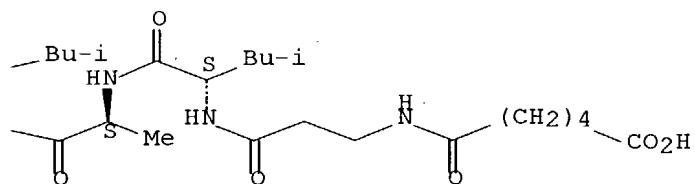
CN L-Leucinamide, N-(5-carboxy-1-oxopentyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



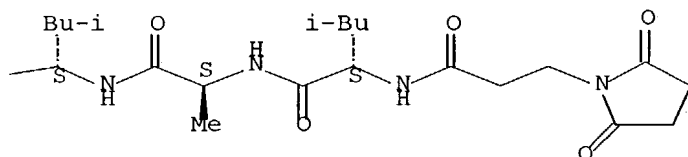
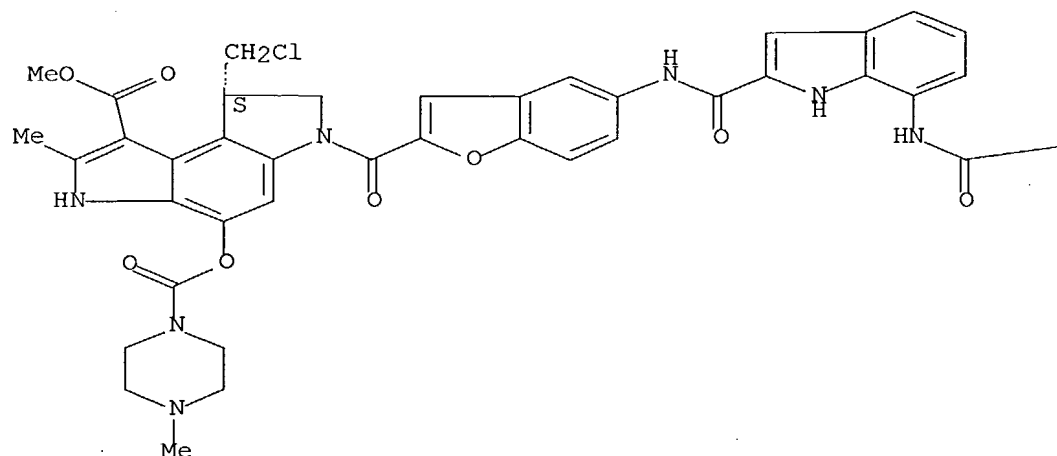
PAGE 1-B



RN 477209-65-7 CAPLUS

CN L-Leucinamide, N-[3-(2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-L-leucyl-L-alanyl-N-[2-[[[2-[[[2-[[[1S]-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[4-methyl-1-piperazinyl]carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-66-8 CAPLUS

CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)- β -alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

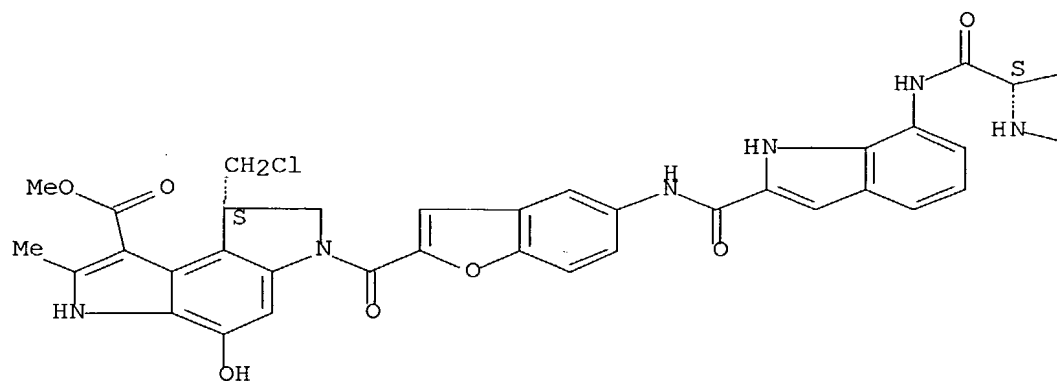
Absolute stereochemistry.

COC(=O)c1c(C)nc2cc(OC(=O)c3ccc(NC(=O)c4c5ccccc4NC(=O)c6c7ccccc6N8C(S8)CCl)cc5)ccc2n1CCCC(=O)N[C@H](CCCC(=O)N[C@@H](CCCC(=O)N)C)C(=O)NCCCC(=O)OCN1CCCCN1

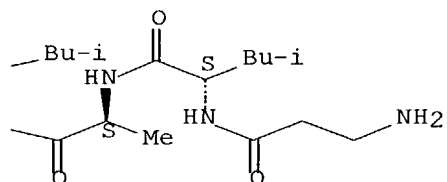
CN L-Leucinamide, β -alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[1S]-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

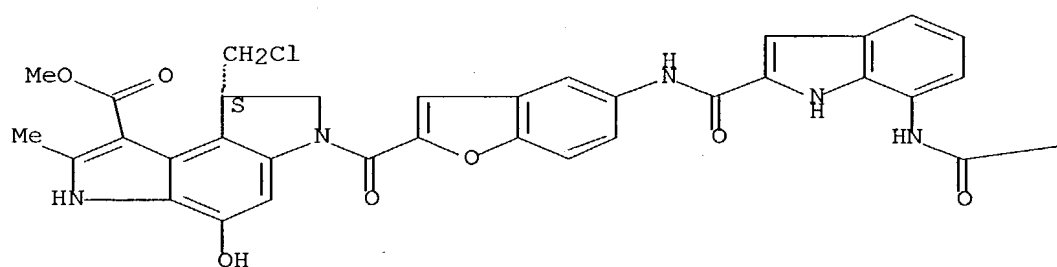


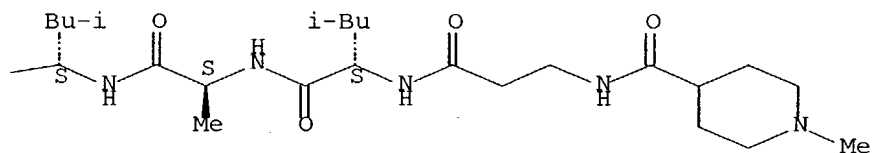
RN 477209-68-0 CAPLUS

CN L-Leucinamide, N-[(1-methyl-4-piperidiny)carbonyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[2-[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



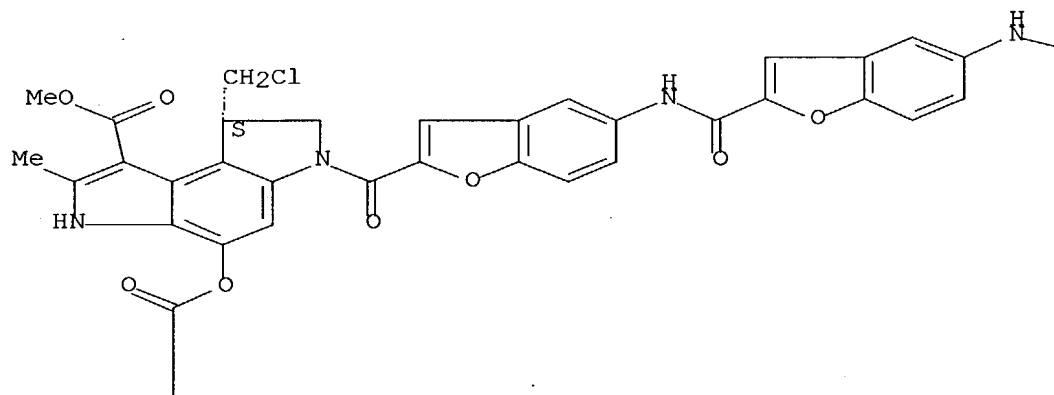


RN 477209-69-1 CAPLUS

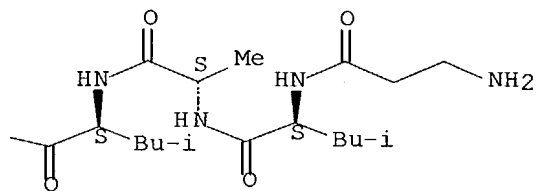
CN L-Leucinamide, β -alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-

5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

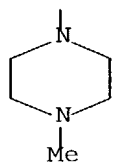
Absolute stereochemistry.



PAGE 1-B



PAGE 2-A

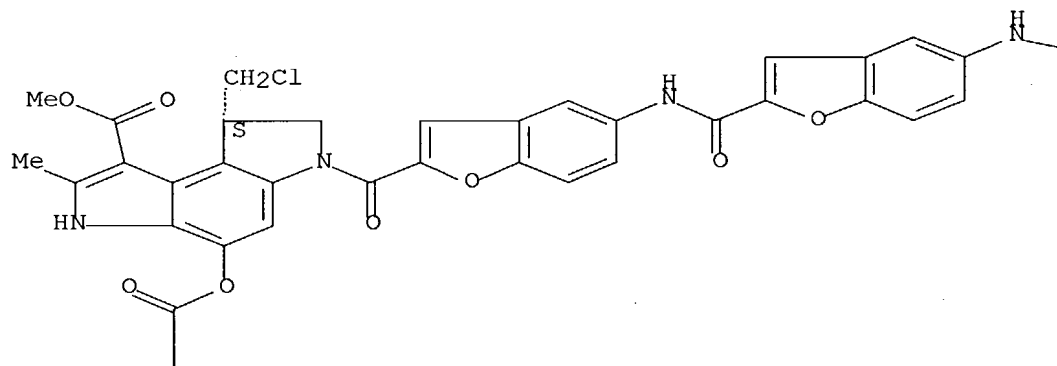


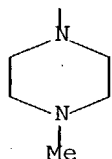
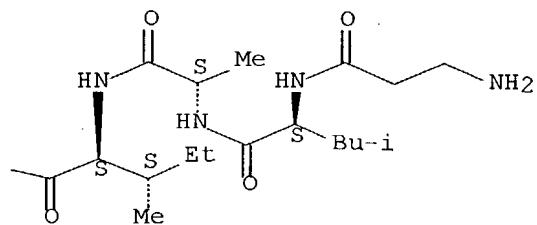
RN 477209-70-4 CAPLUS

CN L-Isoleucinamide, β -alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

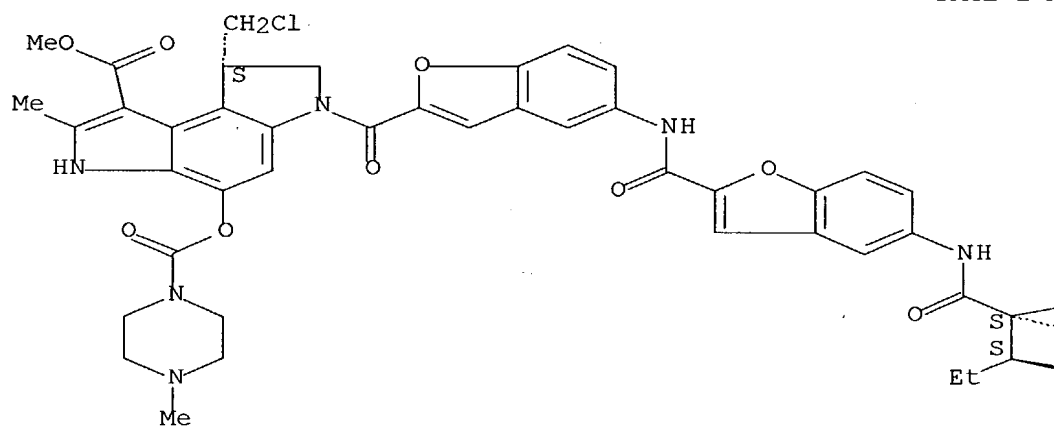


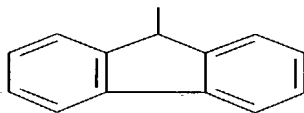
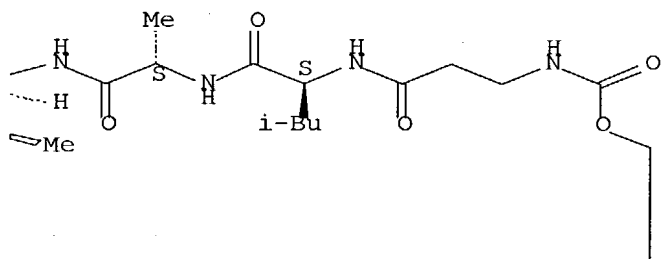


RN 477209-71-5 CAPLUS

CN L-Isoleucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[[4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

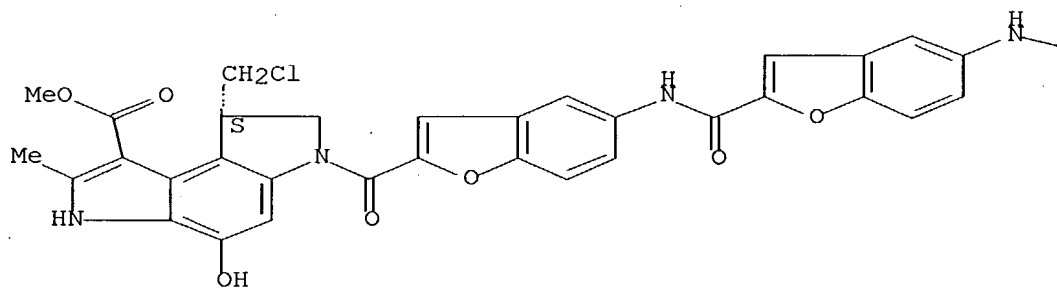


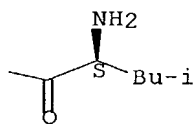


RN 477209-73-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[[5-[[[5-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

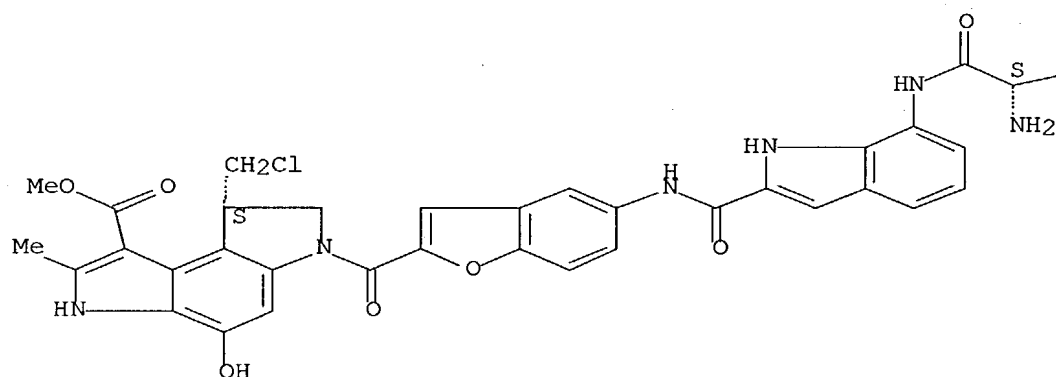




RN 477209-74-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



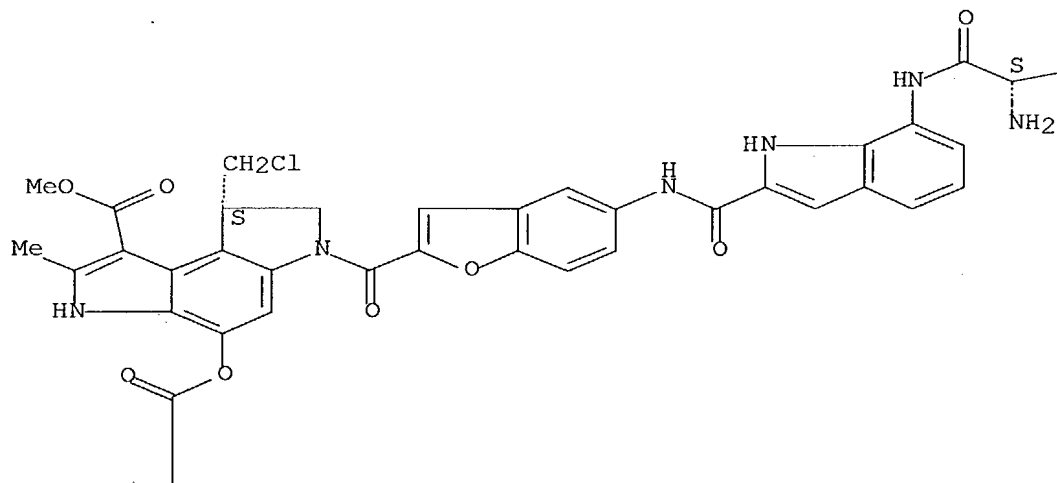
— Bu-i

RN 477209-75-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

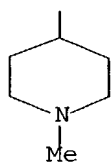
PAGE 1-A



PAGE 1-B

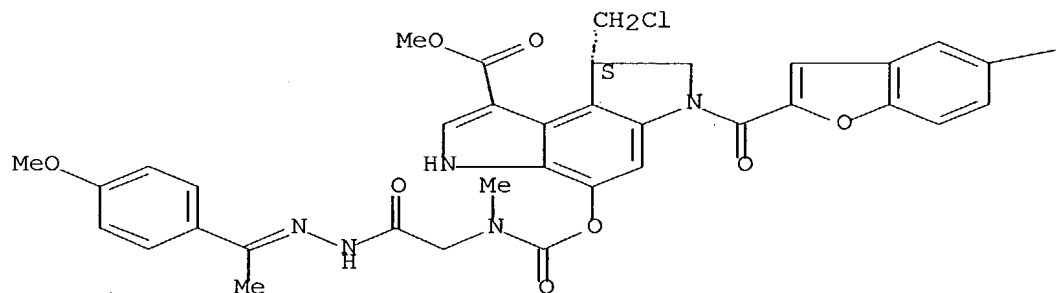
Bu-i

PAGE 2-A



RN 477209-76-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[2-[[1-(4-methoxyphenyl)ethylidene]hydrazino]-2-
 oxoethyl]methylamino]carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

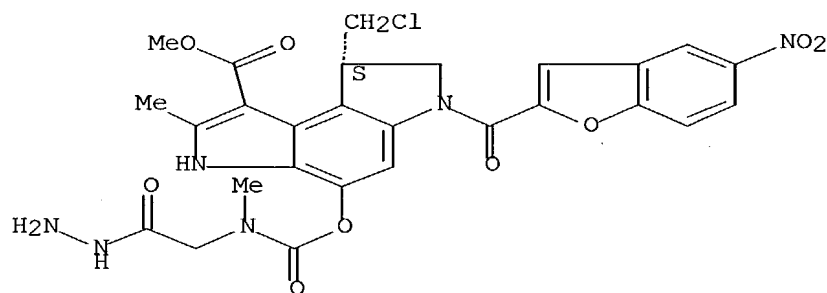
Absolute stereochemistry.
 Double bond geometry unknown.



—NO2

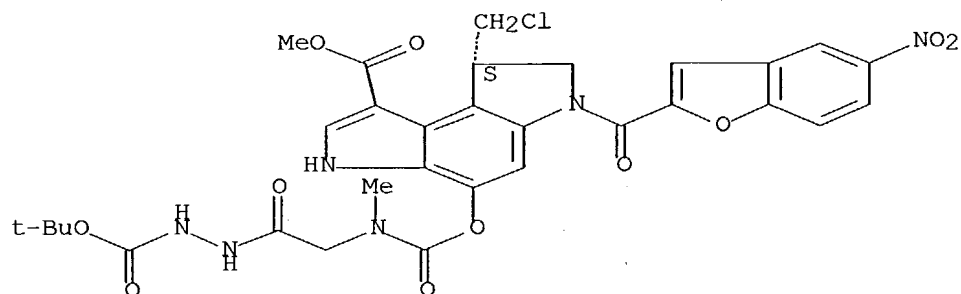
RN 477209-77-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[[(2-
 hydrazino-2-oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-
 methyl-
 6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



RN 477209-78-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[[[2-
 [2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-
 oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-nitro-2-
 benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-79-3 CAPLUS

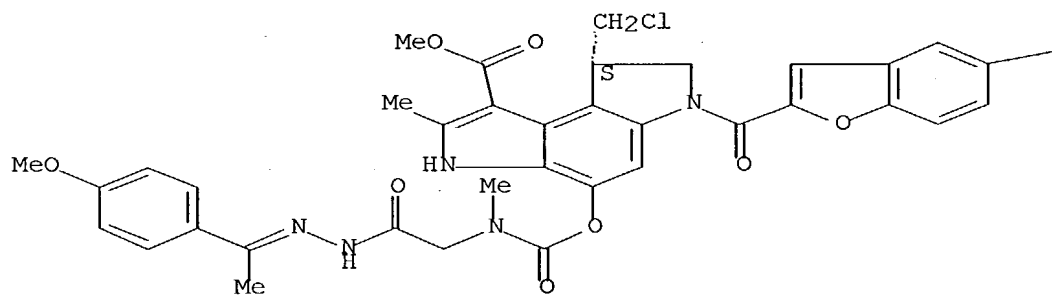
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[[2-[[1-(4-methoxyphenyl)ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

—NO2

RN 477209-80-6 CAPLUS

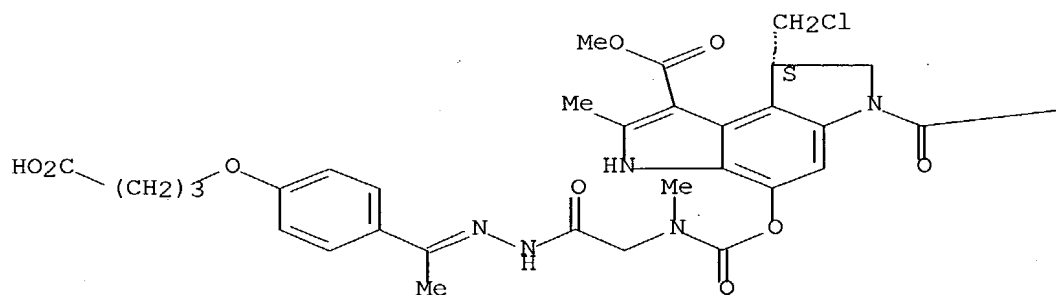
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[[1-[4-(3-carboxypropoxy)phenyl]ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-

6-

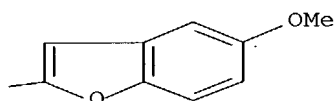
[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



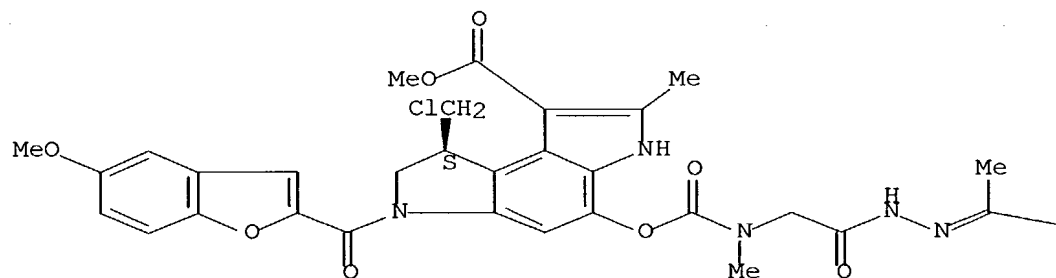
PAGE 1-B

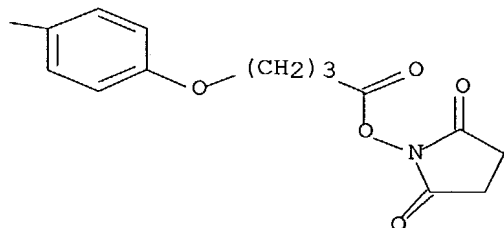


RN 477209-81-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[[2-
[[1-[4-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-
oxobutoxy]phenyl]ethylidene]hy
drazino]-2-oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-
methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

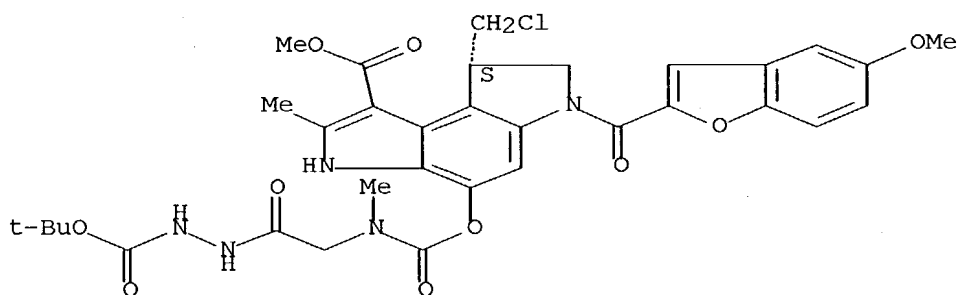
PAGE 1-A





RN 477209-82-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [2-
 [2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-
 oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-
 benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX
 NAME)

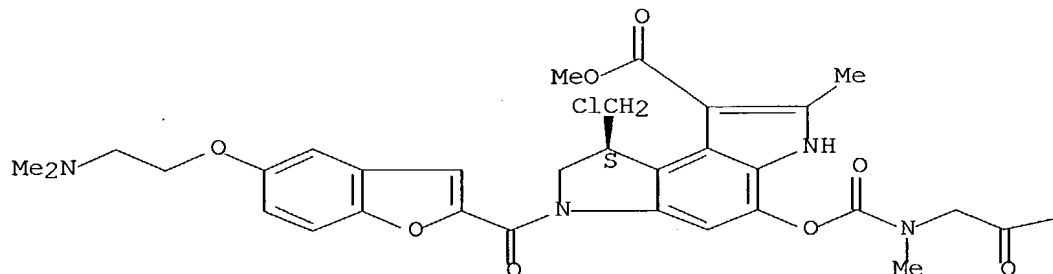
Absolute stereochemistry.



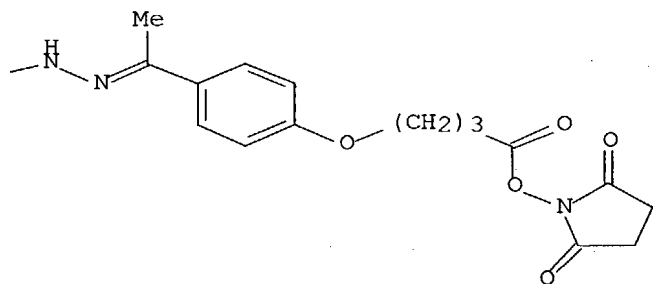
RN 477209-83-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
 [2-
 (dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[2-[[1-[4-[4-[(2,5-
 dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-2-
 oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl
 ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

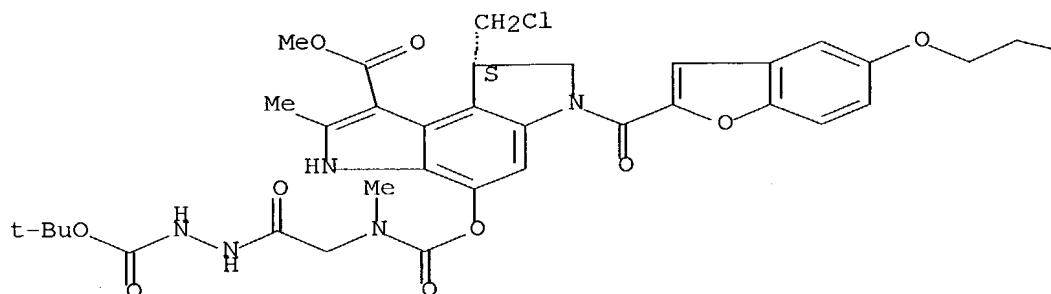


RN 477209-84-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
[2-

(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[2-[2-[(1,1-
dimethylethoxy)carbonyl]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-
3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

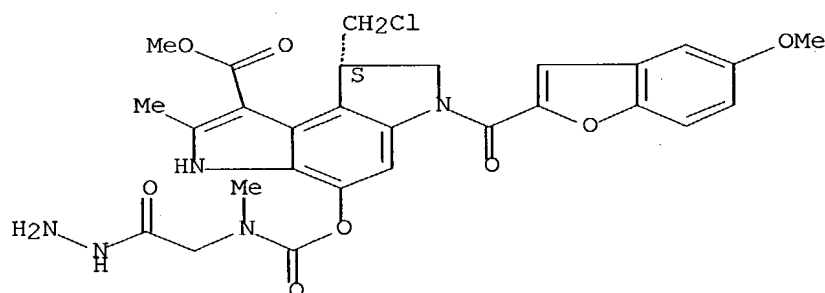
Absolute stereochemistry.



—NMe₂

RN 477209-85-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(2-
 hydrazino-2-oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-
 methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI)
 (CA INDEX NAME)

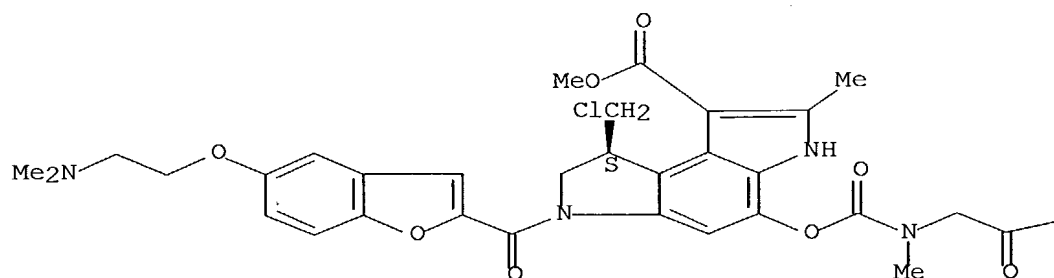
Absolute stereochemistry.



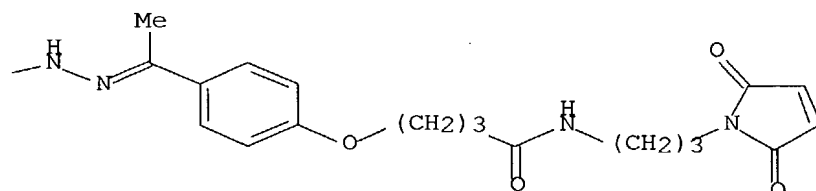
RN 477209-86-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(2-
 [[1-[4-[4-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]amino]-4-
 oxobutoxy]phenyl]ethylidene]hydrazino]-2-
 oxoethyl)methylamino]carbonyl]oxy
]-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-
 tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

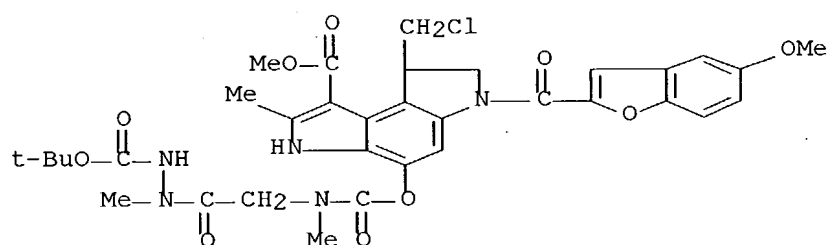


RN 477209-87-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-

[[[[2-

[2-[(1,1-dimethylethoxy)carbonyl]-1-methylhydrazino]-2-oxoethyl]methylamino]carbonyloxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 477209-88-4 CAPLUS

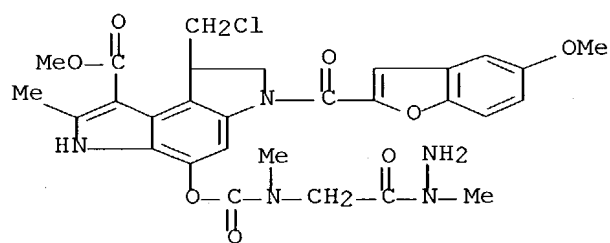
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-

[[[methyl[2-

(1-methylhydrazino)-2-oxoethyl]amino]carbonyl]oxy]-, methyl ester (9CI)

(CA INDEX NAME)



RN 477209-89-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-

[[[2-

[[[1-[4-[4-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]amino]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-2-

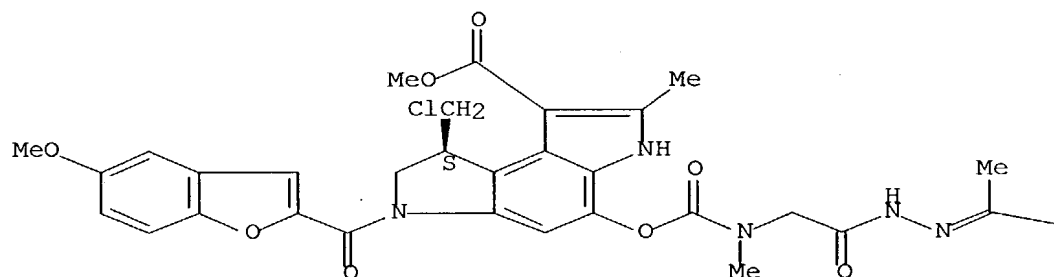
oxoethyl]methylamino]carbonyl]oxy

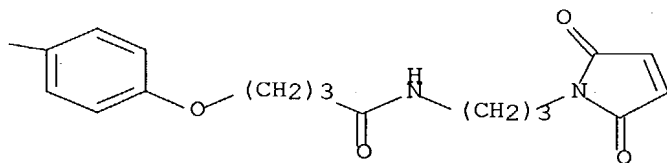
]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

PAGE 1-A





RN 477209-90-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[2-

[[1-[4-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]me

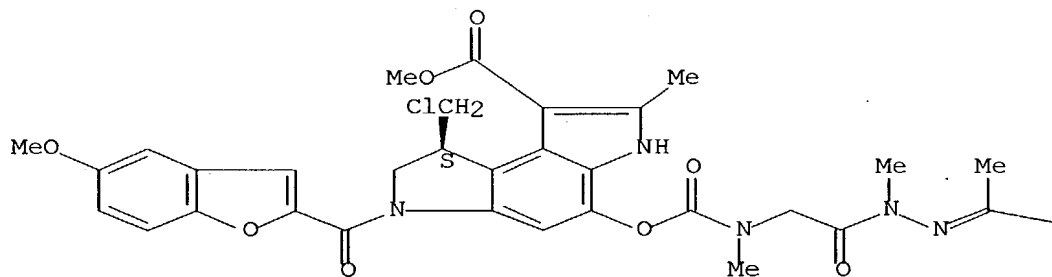
thylhydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-

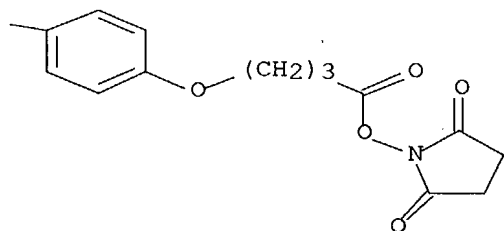
6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)-(9CI)

(CA INDEX NAME)

Absolute stereochemistry.

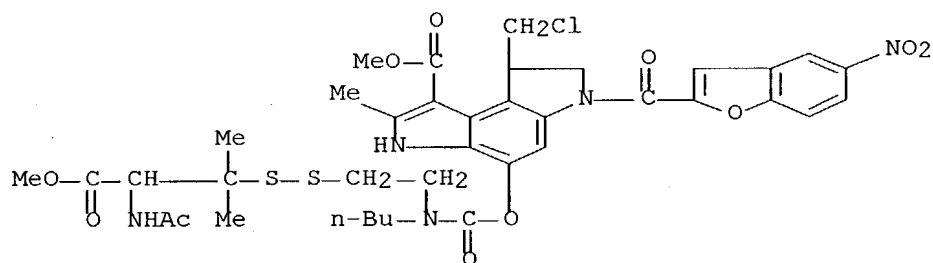
Double bond geometry unknown.





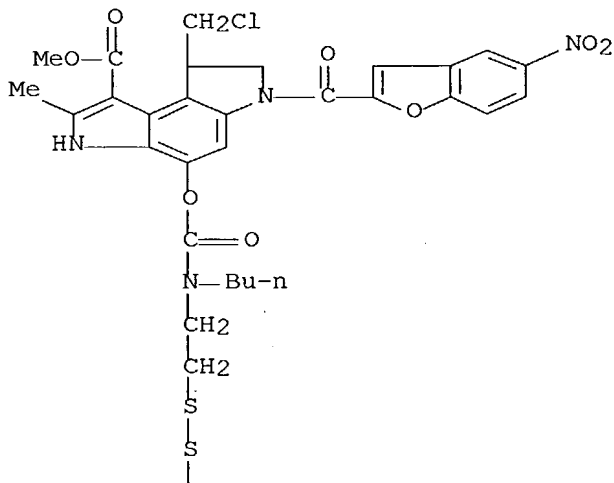
RN 477209-91-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[[2-(acetylamino)-3-methoxy-1,1-dimethyl-3-oxopropyl]dithio]ethyl]butylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



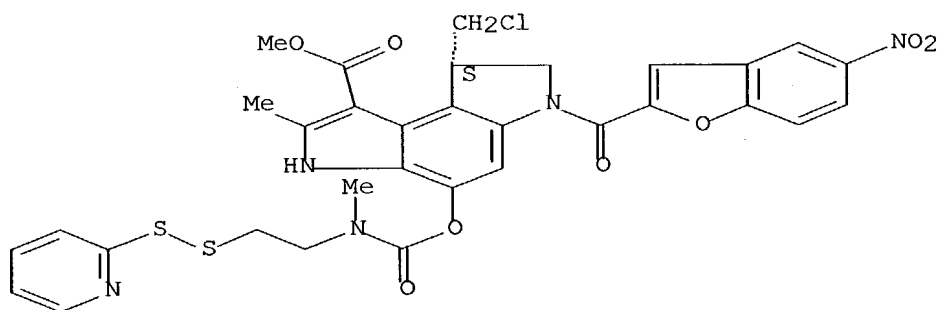
RN 477209-92-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-(2-pyridinyldithio)ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 477209-93-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-(2-pyridinyldithio)ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

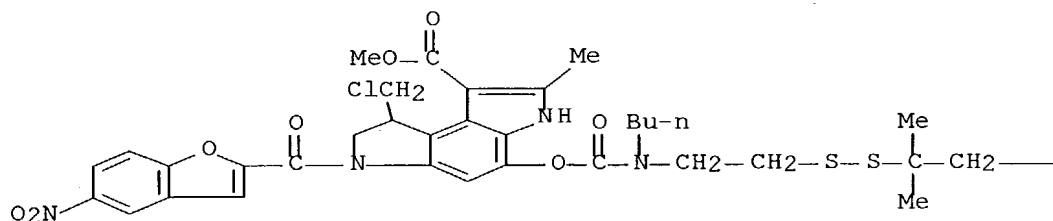
Absolute stereochemistry.



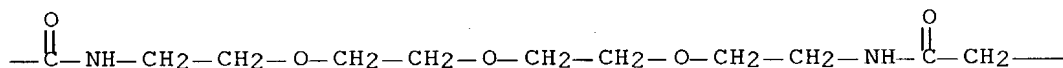
RN 477209-94-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[2-butyl-25-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-7,7-dimethyl-1,9,23-trioxo-13,16,19-trioxa-5,6-dithia-2,10,22-triazapentacos-1-yl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

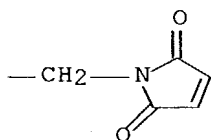
PAGE 1-A



PAGE 1-B



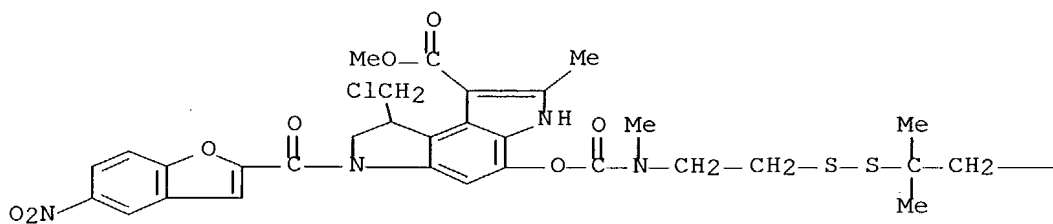
PAGE 1-C



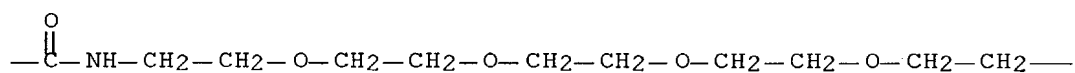
RN 477209-95-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[31-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-2,7,7-trimethyl-1,9,29-trioxo-13,16,19,22,25-pentaoxa-5,6-dithia-2,10,28-triazahentriacont-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

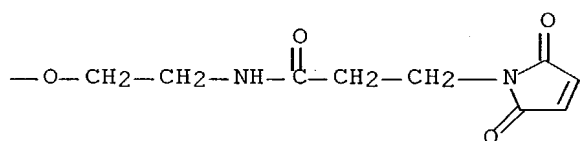
PAGE 1-A



PAGE 1-B



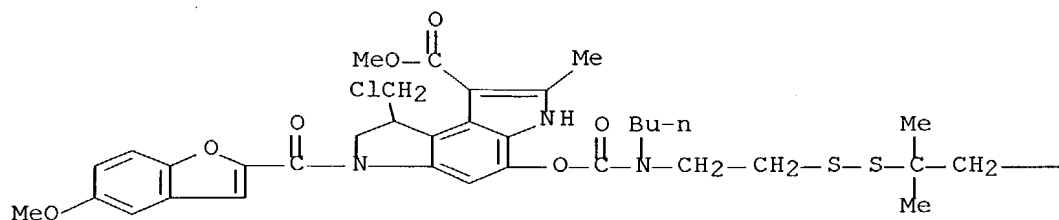
PAGE 1-C



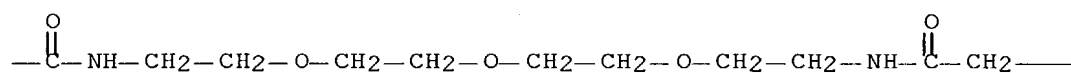
RN 477209-96-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[2-butyl-25-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-7,7-dimethyl-1,9,23-trioxo-13,16,19-trioxa-5,6-dithia-2,10,22-triazapentacos-1-yl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

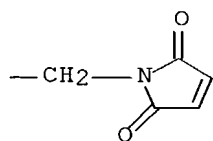
PAGE 1-A



PAGE 1-B



PAGE 1-C



RN 477209-97-5 CAPLUS

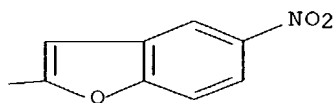
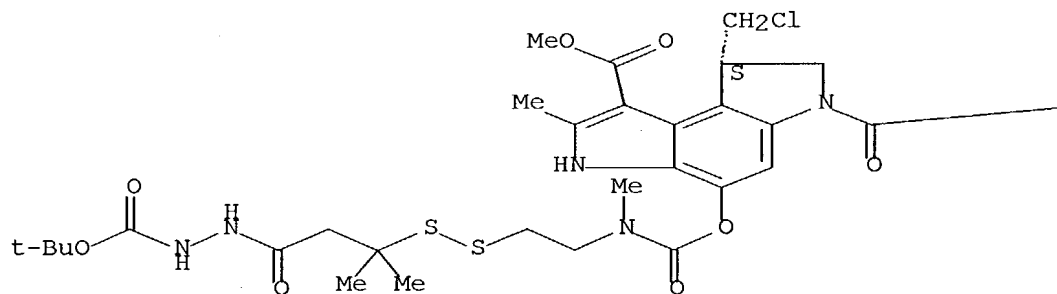
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-4-

[(2,7,7,14,14-

pentamethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-yl)oxy]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



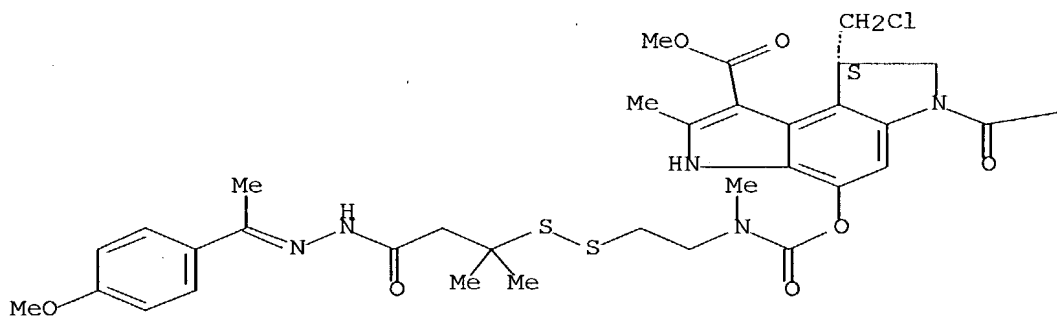
RN 477209-98-6 CAPLUS

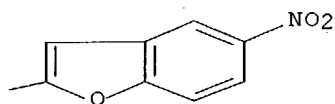
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[[2-[[3-[[1-(4-methoxyphenyl)ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.





RN 477209-99-7 CAPLUS

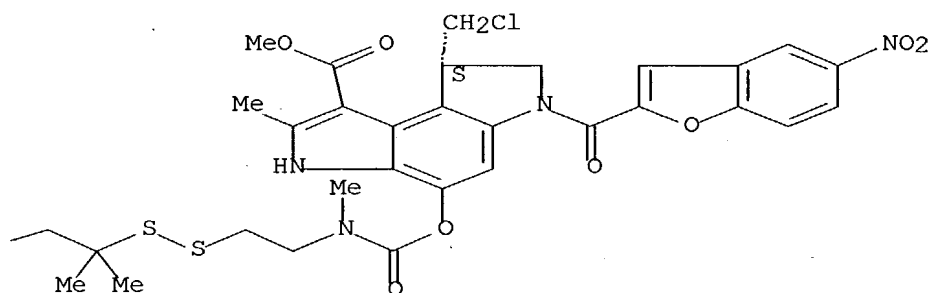
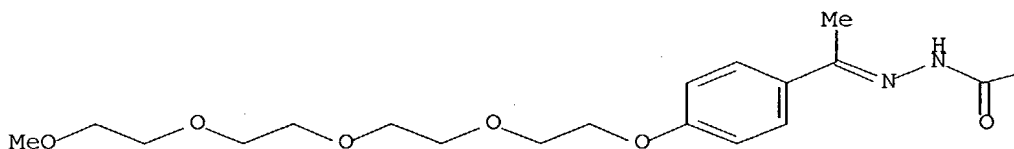
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[2-

[[1,1-dimethyl-3-oxo-3-[[1-[4-(3,6,9,12-tetraoxatridec-1-

yl oxy)phenyl]ethylidene]hydrazino]propyl]dithio]ethyl]methylamino]carbonyl
oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

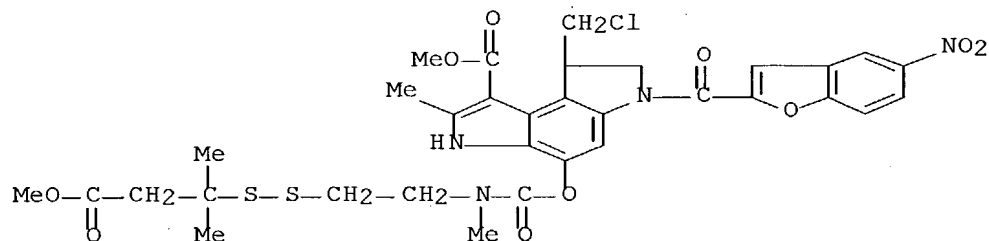
Absolute stereochemistry.

Double bond geometry unknown.



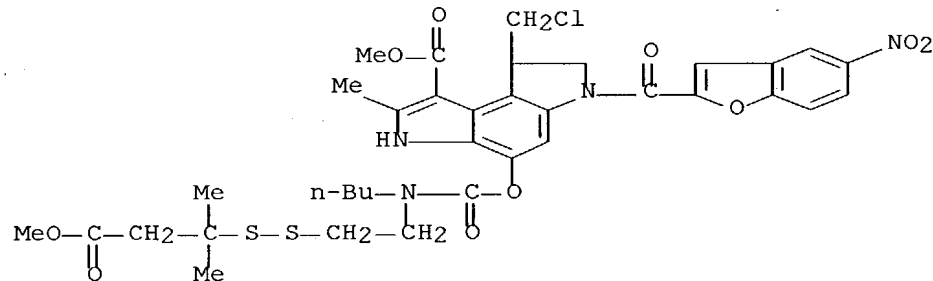
RN 477210-00-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-[[[2-[(3-methoxy-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 477210-01-8 CAPLUS

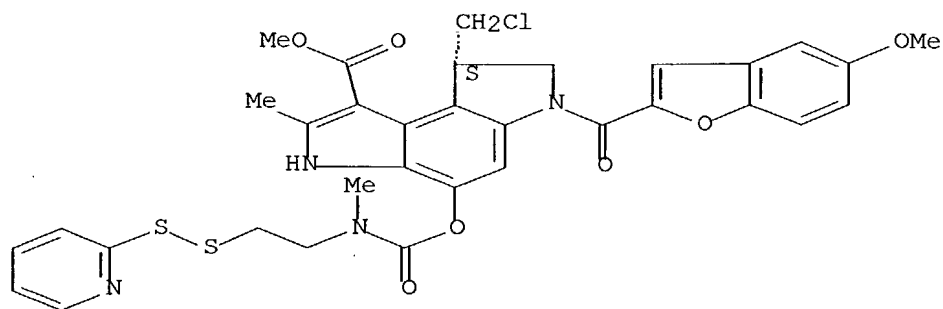
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(3-methoxy-1,1-dimethyl-3-oxopropyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-
3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 477210-02-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-2-methyl-6-[(5-methoxy-2-benzofuranyl)carbonyl]-4-[[[methyl[2-(2-pyridinyldithio)ethyl]amino]carbonyl]oxy]-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

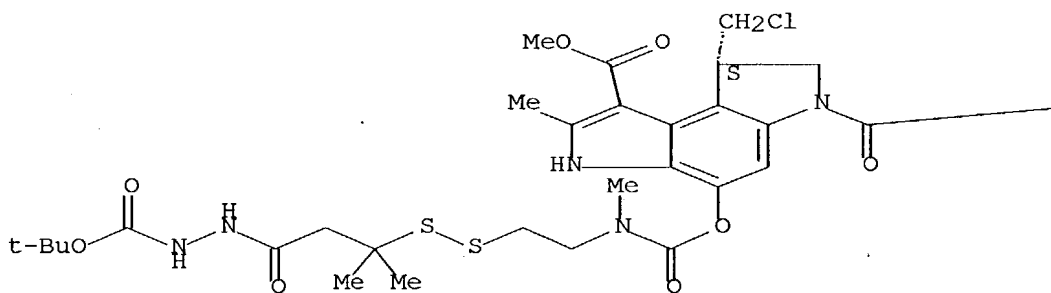
Absolute stereochemistry.



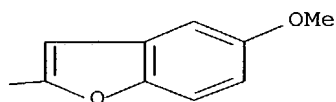
RN 477210-03-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-
 [(2,7,7,14,14-
 pentamethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-
 yl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

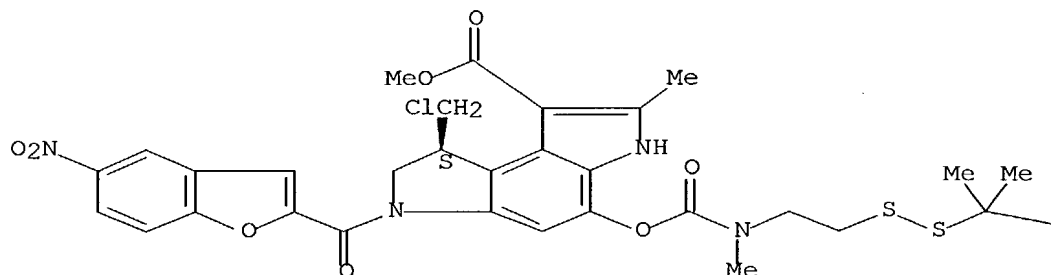


RN 477210-04-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[[[[2-
 [[3-[[1-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-
 yl)phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-
 oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-

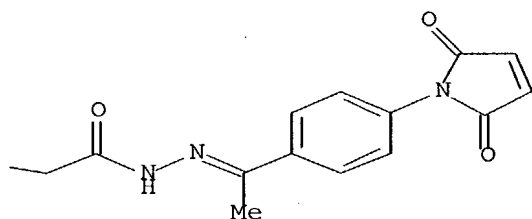
methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



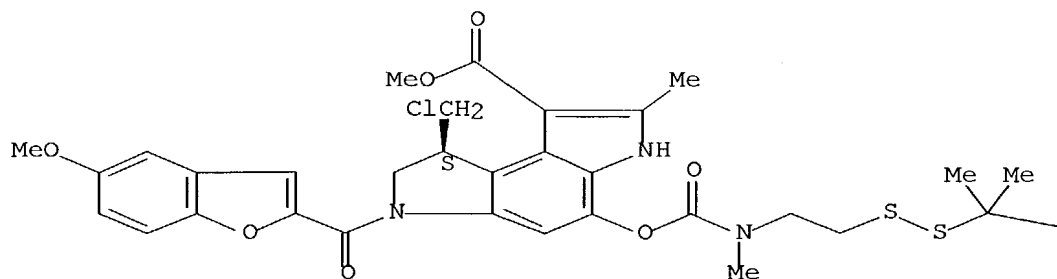
PAGE 1-B



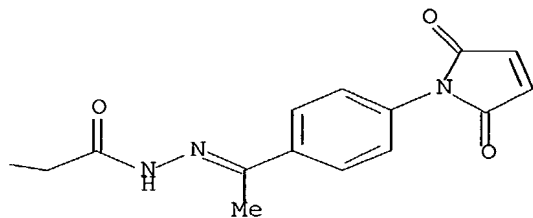
RN 477210-05-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[[2-
[[3-[[1-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-
yl)phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-
oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-
[(5-
methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



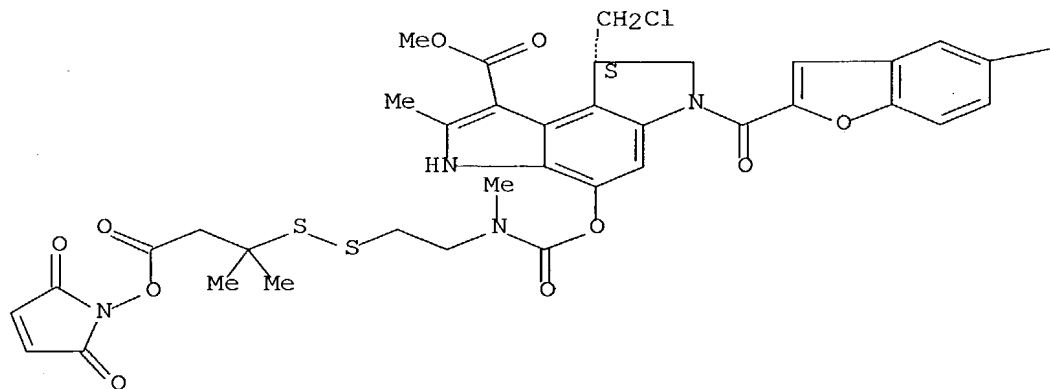
RN 477210-06-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[[2-

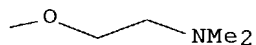
[[3-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)oxy]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



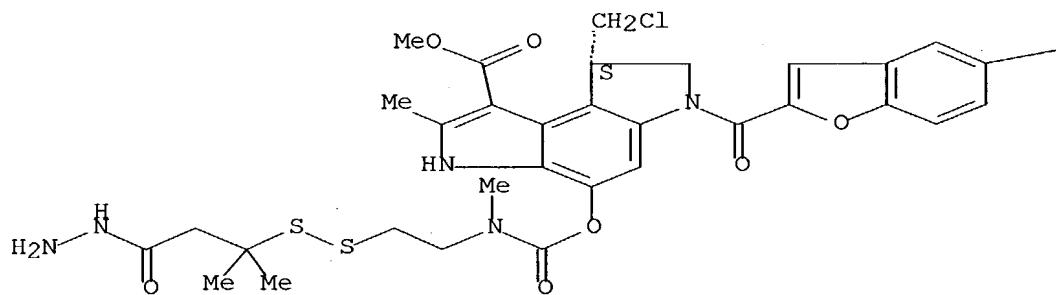
PAGE 1-B



RN 477210-07-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[[[2-
 [(3-hydrazino-1,1-dimethyl-3-
 oxopropyl)dithio]ethyl]methylamino]carbonyl]o
 xy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-,
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



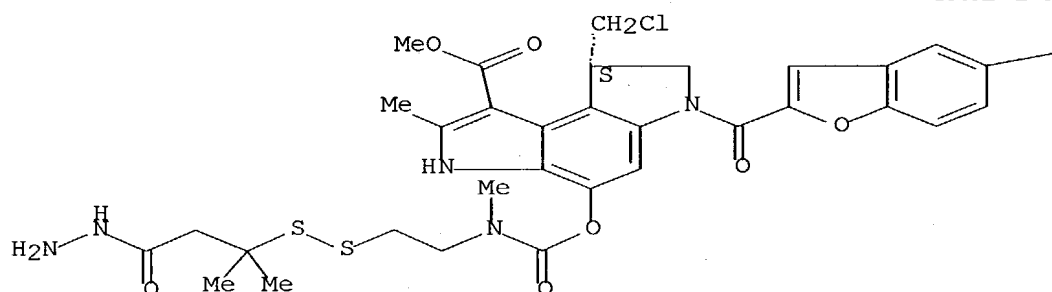
—NO2

RN 477210-08-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
[[[2-

[(3-hydrazino-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]oxy-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

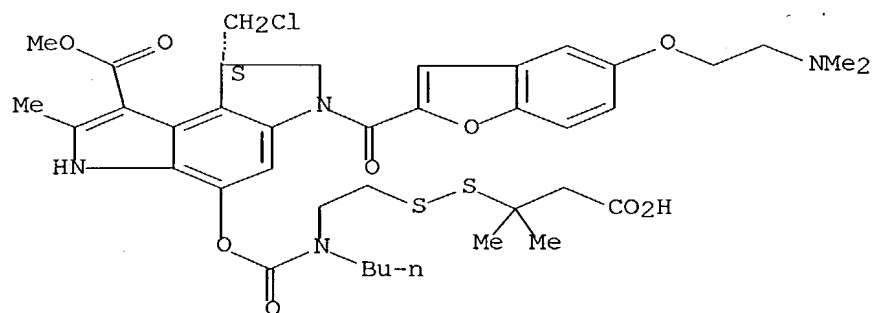


—OMe

RN 477210-09-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

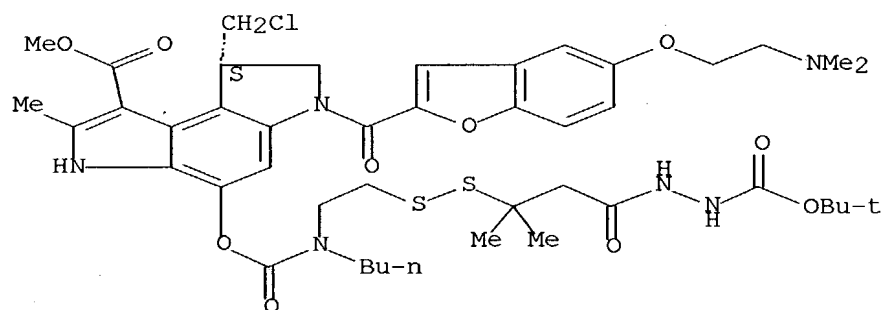
Absolute stereochemistry.



RN 477210-10-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[(2-butyl-7,7,14,14-tetramethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-yl)oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

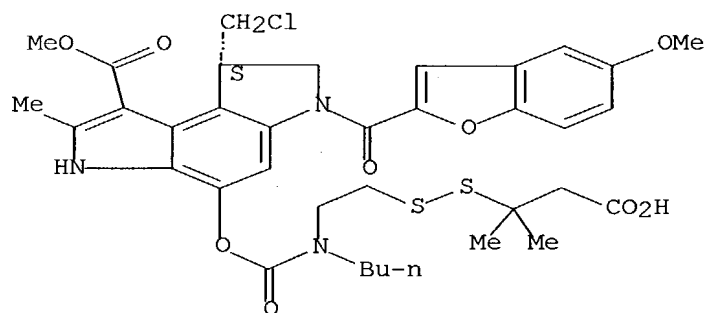
Absolute stereochemistry.



RN 477210-11-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)-(9CI) (CA INDEX NAME)

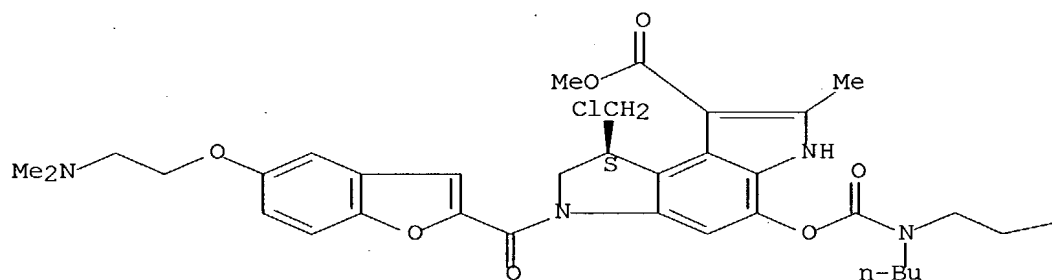
Absolute stereochemistry.



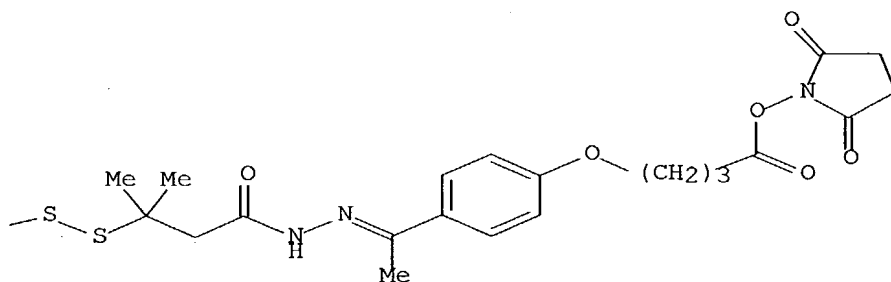
RN 477210-12-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[[3-[[1-[4-[4-
 [(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

PAGE 1-A



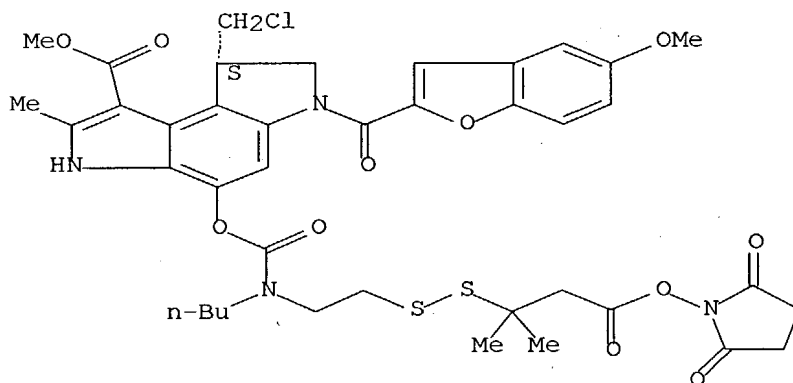
PAGE 1-B



RN 477210-13-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

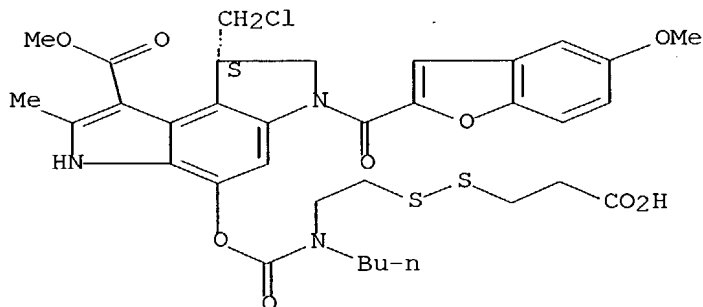
Absolute stereochemistry.



RN 477210-14-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxyethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

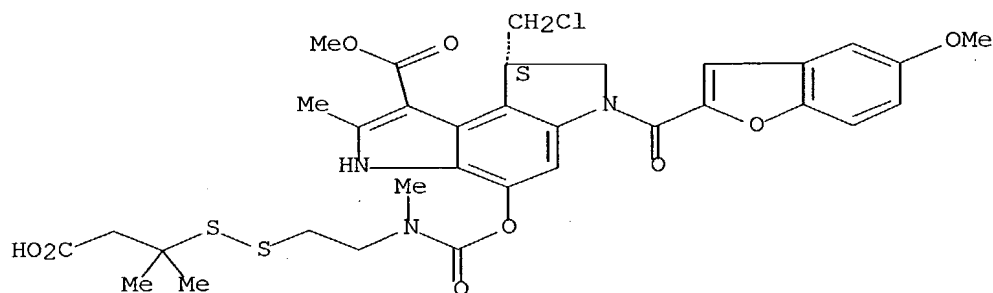


RN 477210-15-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-

3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-,
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

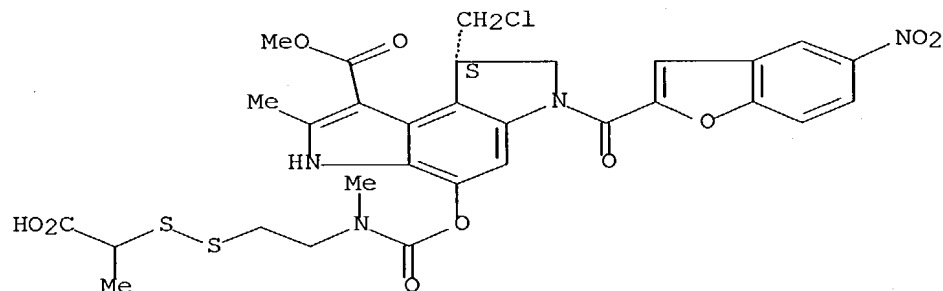
Absolute stereochemistry.



RN 477210-16-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(1-carboxyethyl)dithio]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

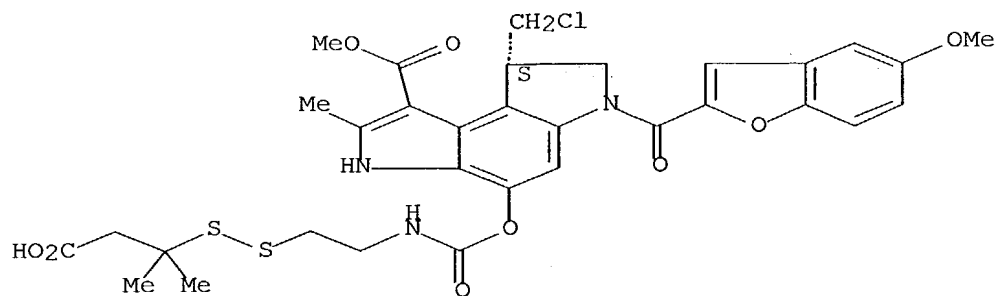
Absolute stereochemistry.



RN 477210-17-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

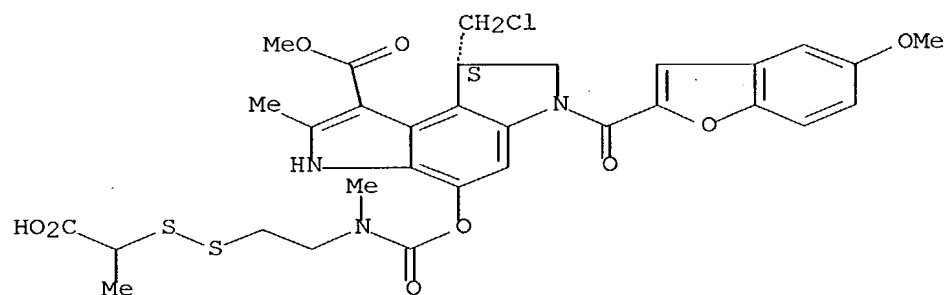
Absolute stereochemistry.



RN 477210-18-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(1-carboxyethyl)dithio]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

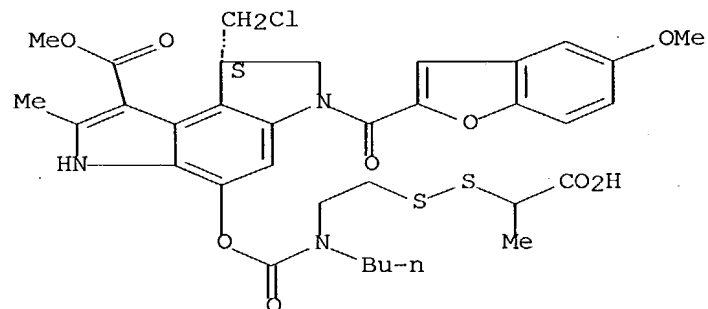
Absolute stereochemistry.



RN 477210-19-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-carboxyethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

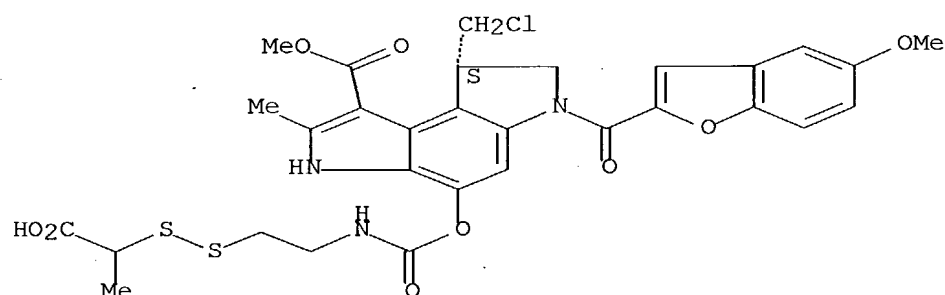
Absolute stereochemistry.



RN 477210-20-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[2-[(1-carboxyethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

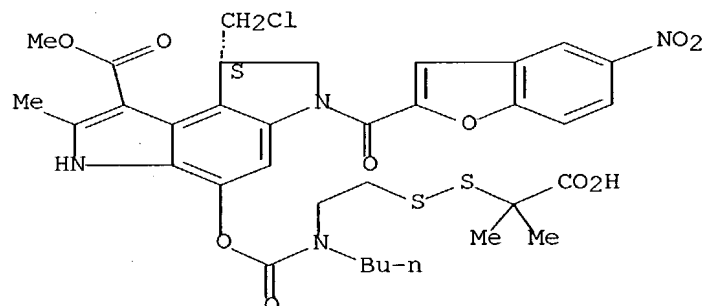
Absolute stereochemistry.



RN 477210-21-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

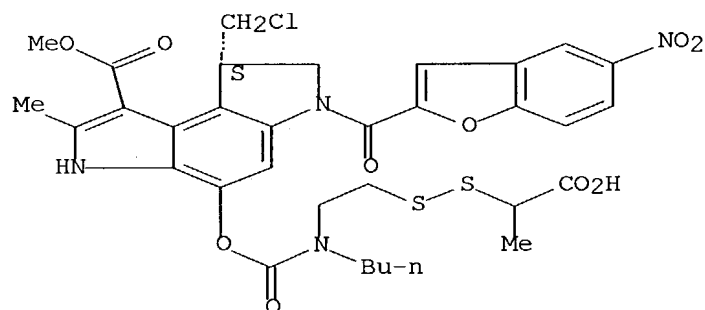
Absolute stereochemistry.



RN 477210-22-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-carboxylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

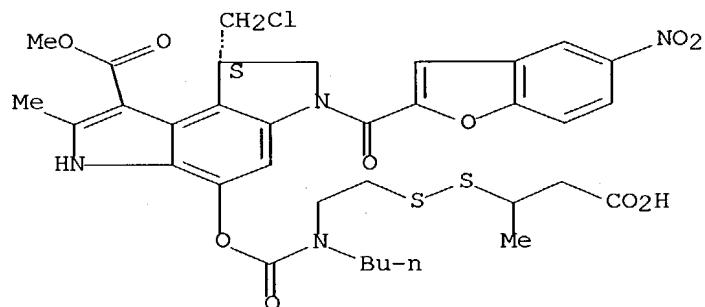
Absolute stereochemistry.



RN 477210-23-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

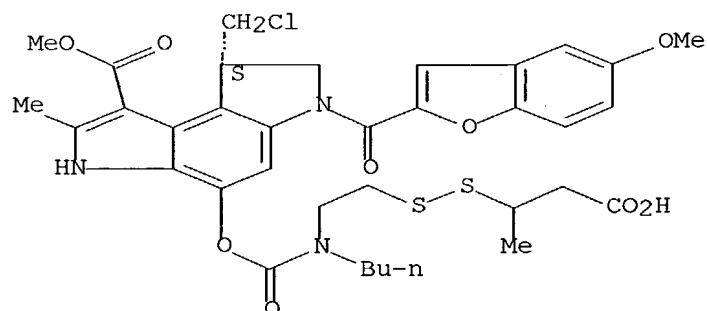
Absolute stereochemistry.



RN 477210-24-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

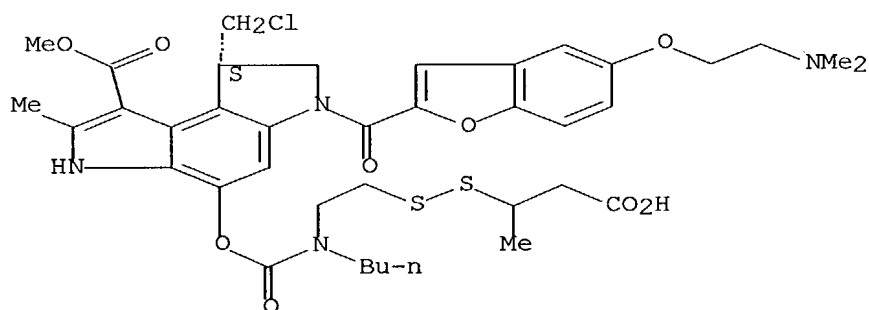
Absolute stereochemistry.



RN 477210-25-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

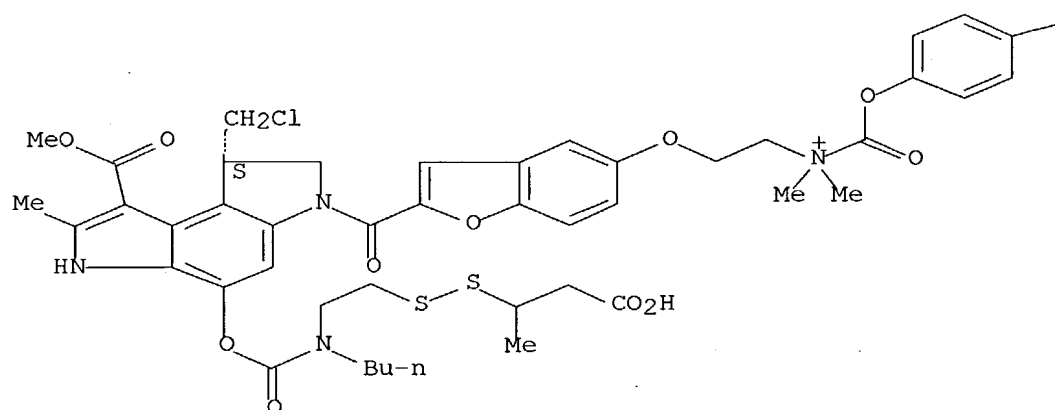
Absolute stereochemistry.



RN 477210-26-7 CAPLUS

CN Ethanaminium, 2-[[2-[[[(1S)-5-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]oxy]-N,N-dimethyl-N-[(4-nitrophenoxycarbonyl)-5-benzofuranyl]ethanaminium, (9CI) (CA INDEX NAME)

Absolute stereochemistry.

—NO₂

RN 477210-27-8 CAPLUS

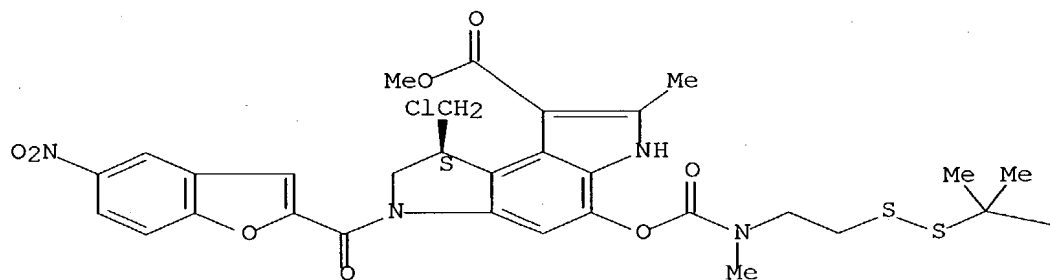
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-

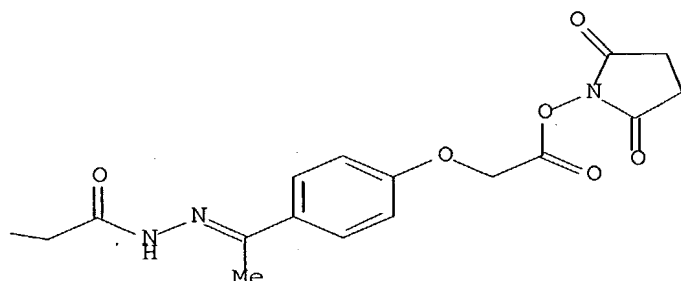
[[[2-

[[3-[[1-[4-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethoxy]phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

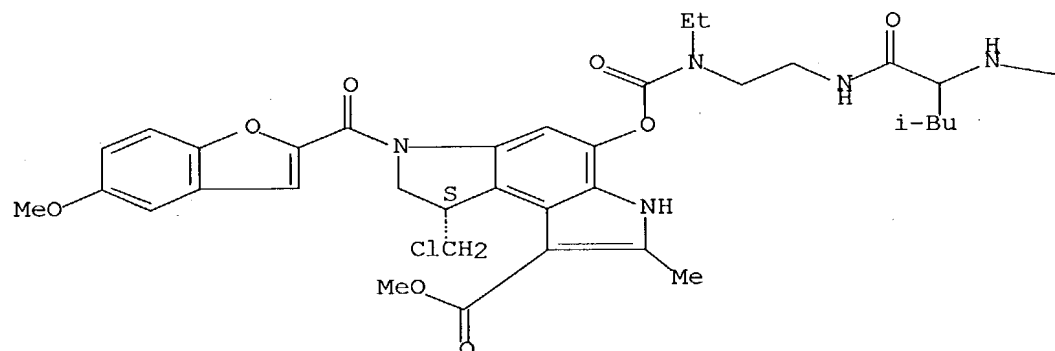


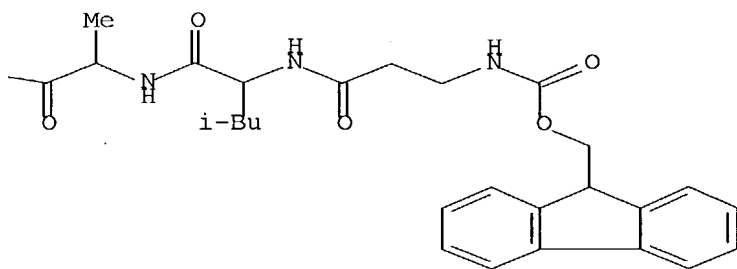


RN 477328-57-7 CAPLUS

CN Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]- β -
 alanylleucylalanyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-6-
 [(5-methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-methylbenzo[1,2-
 b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

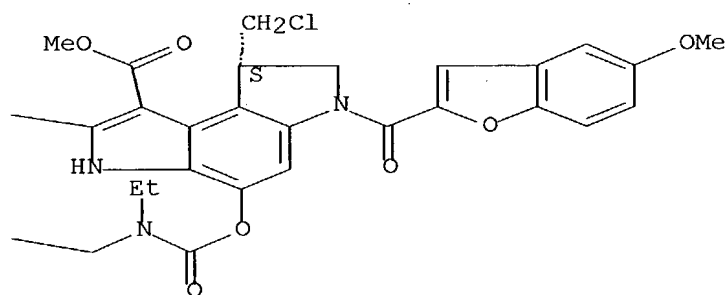
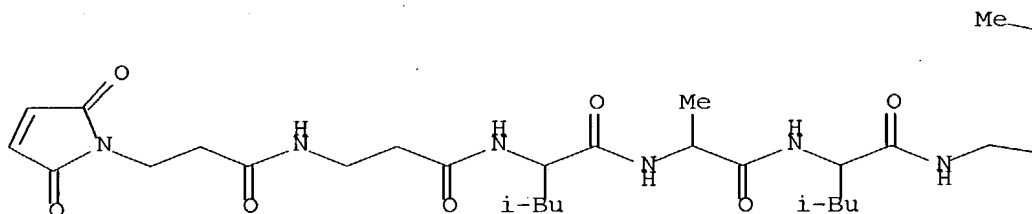




RN 477328-58-8 CAPLUS

CN Leucinamide, N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-
 β -alanylleucylalanyl-N-[2-[[[(8S)-8-(chloromethyl)-3,6,7,8-
 tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-
 methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477328-64-6 CAPLUS

CN Leucinamide, N-(3-carboxy-1-oxopropyl)- β -alanylleucylalanyl-N-[6-[[2-
[[[2-[[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-

7-

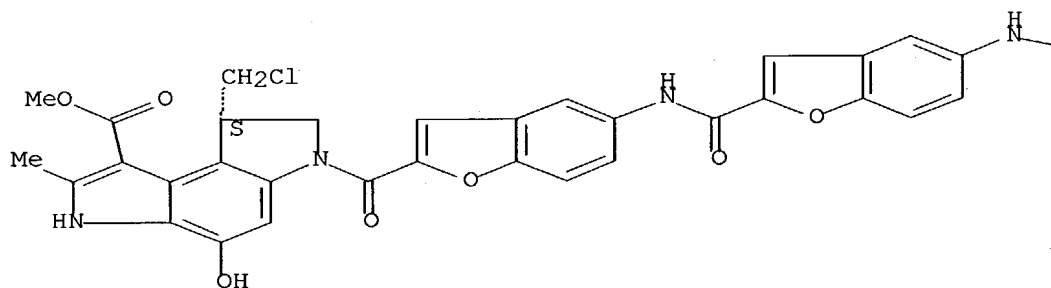
methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-
benzofuranyl]amino]carbonyl]-5-benzofuranyl]amino]-6-oxohexyl]- (9CI)

(CA

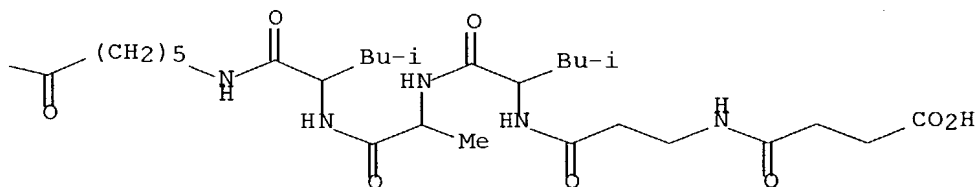
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:755199 CAPLUS Full-text

DN 137:284323

TI Enzyme-cleavable prodrug compounds

IN Dubois, Vincent; Fernandez, Anne Marie; Gangwar, Sanjeev; Lewis, Evan;
Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Lesley B.; Trouet, Andre;
Yarranton, Geoffrey T.

PA Belg.

SO U.S. Pat. Appl. Publ., 86 pp., Cont.-in-part of Appl. No.

PCT/US99/30393.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002142955	A1	20021003	US 2001-879442	20010611
	WO 2000033888	A2	20000615	WO 1999-US30393	19991210
	WO 2000033888	A3	20011108		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	US 1998-111793P	P	19981211
	US 1999-119312P	P	19990208
	WO 1999-US30393	A2	19991210
	US 2000-211887P	P	20000614
	US 2001-290448P	P	20010511

OS MARPAT 137:284323

AB The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme Thimet oligopeptidase, or TOP. Also disclosed are methods of designing prodrugs by utilizing TOP-cleavable sequences within the conjugate and methods of treating patients with prodrugs of the invention.

IT **154889-68-6**, Kw-2189

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thimet oligopeptidase-cleavable prodrug compds.)

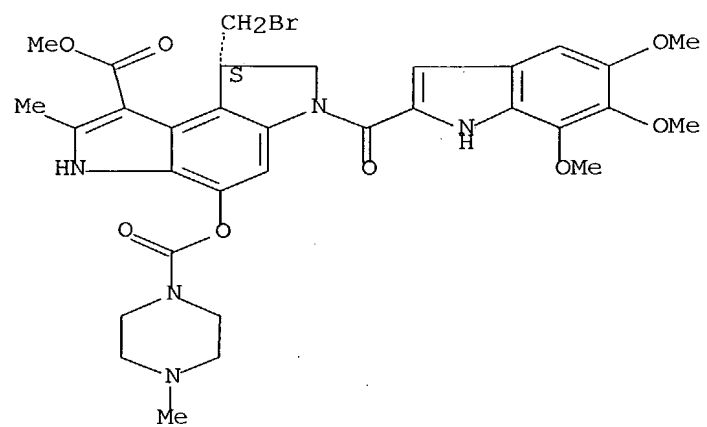
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



L10 ANSWER 10 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:512270 CAPLUS Full-text

DN 138:153386

TI Novel furano analogues of duocarmycin C1 and C2: design, synthesis, and biological evaluation of seco-iso-Cyclopropylfurano[2,3-e]indoline (seco-iso-CFI) and seco-Cyclopropyltetrahydrofurano[2,3-f]quinoline (seco-CFQ) analogues

AU Howard, Tiffany T.; Lingerfelt, Brian M.; Purnell, Bethany L.; Scott, Adrienne E.; Price, Carly A.; Townes, Heather M.; McNulty, LuAnne;

Handl,

Heather L.; Summerville, Kaitlin; Hudson, Stephen J.; Bowen, J. Phillip; Kiakos, Konstantinos; Hartley, John A.; Lee, Moses

CS Department of Chemistry, Furman University, Greenville, SC, 29613, USA

SO Bioorganic & Medicinal Chemistry (2002), 10(9), 2941-2952

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

OS CASREACT 138:153386

AB The design, synthesis and biol. evaluation of novel seco-iso-cyclopropylfurano[2,3-e]indoline (seco-iso-CFI) and the seco-cyclopropyltetrahydrofurano[2,3-f]quinoline (seco-CFQ) analogs of the duocarmycins are described. These novel analogs were designed on the premise that the lone pair of electrons on the furano-oxygen atom could enter into conjugation with the isocyclopropylfurano[e]indolone (iso-CFI) alkylating moiety, formed from the loss of HCl in these compds. The seco-iso-CFI DNA alkylating pharmacophore was synthesized through a well precededented approach of 5-exo-trig aryl radical cyclization with a vinyl chloride. In our studies, in addition to the formation of the seco-iso-CFI product, an equal amount of an unexpected seco-CFQ product was also generated during the radical cyclization reaction. Like CC-1065 and adozelesin, using Taq DNA polymerase stop and thermal cleavage assays, the seco-iso-CFI compds. and the seco-CFQ compds. were shown to preferentially alkylate the adenine-N3 position within the minor groove of long stretches of A residues. A MM2 energy optimized mol. model of a 1:1 complex of one compound with DNA reveals that the iso-CFI compound fits snugly within the minor groove. Using a MTT based experiment, the cytotoxicity of these compds. were determined against the growth of murine leukemia (L1210), mastocytoma (P815) and melanoma (B16) cell lines. The concns. of compds. required to inhibit the growth of these tumor cells by 50% is in the range of 10⁻⁸ M. These compds. were also tested against a panel of human cancer cells by the National Cancer Institute, demonstrating that the compds. exhibited a high level of activity against selected solid tumors. At a concentration of 0.0084 μ M (based on the IC50 of one compound (seco-CBI-TMI) against the growth L1210 cells), while some other compds. were toxic against murine bone marrow cells as judged by a colony forming study of freshly isolated murine progenitor hematopoietic cells, compound 5, a seco-CFQ compound, was significantly less toxic. Flow cytometric anal. of P815 cells that had been incubated for 24 h with compds. 4 and 5 at their cytotoxic IC50 concns. indicated the induction of apoptosis in a large percentage of cells, thereby suggesting that this might be the mechanism by which the iso-CFI compds. kill cells.

IT **118292-36-7DP**, Duocarmycin C2, furano analogs

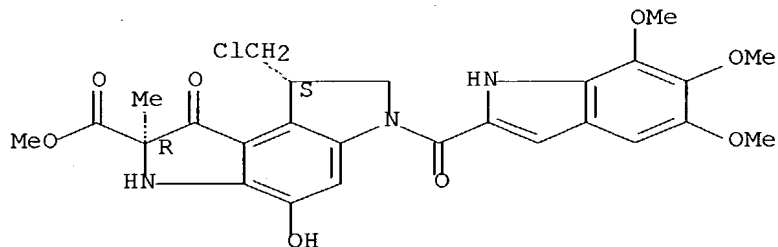
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of cyclopropylfuranoindoline and
cyclopropyltetrahydrofuranoin-
doline as analogs of duocarmycins and their biol. activity as
antitumor
agents)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

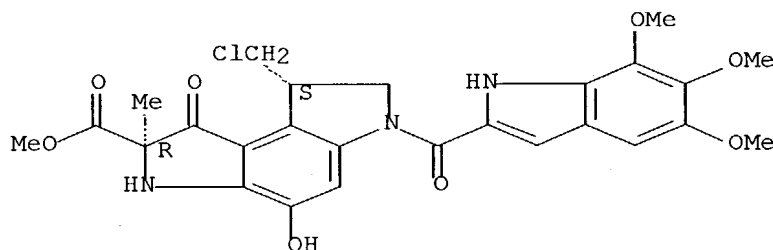
Absolute stereochemistry.



RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:430673 CAPLUS Full-text
 DN 137:362273
 TI Duocarmycins - nature's prodrugs?
 AU Searcey, Mark
 CS Dept. of Pharmaceutical and Biological Chemistry, University of London
 School of Pharmacy, London, WC1N 1AX, UK
 SO Current Pharmaceutical Design (2002), 8(15), 1375-1389
 CODEN: CPDEFP; ISSN: 1381-6128
 PB Bentham Science Publishers
 DT Journal; General Review
 LA English
 AB A review. The duocarmycins and the related (+)-CC-1065 are among the most potent antitumor antibiotics discovered to date, yet they have not progressed to clin. use. These natural products are extremely stable to nucleophilic attack until bound to their DNA target and are not substrates for any other biol. nucleophile. The mechanism of this target activation of the duocarmycins is discussed in relation to both an acid-catalyzed activation and a binding-induced conformational change leading to ground-state destabilization. It is suggested that targeting of the duocarmycins to their site of action in a tumor may be more important than the use of systemically activated prodrugs, as these natural products themselves can be considered to be a type of prodrug, activated only on binding to their targets. Methods that have been used to target CC-1065 and the duocarmycins are reviewed, as well as efforts towards developing systemically activated prodrugs. A simple anal. of the approaches that could be taken to vary the structure for targeting is suggested.
 IT **118292-36-7**, Duocarmycin C2 **124325-94-6**, Duocarmycin B2
 RL: NPO (Natural product occurrence); PAC (Pharmacological activity);
 PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
 (duocarmycins and CC-1065 as naturally occurring prodrugs with antitumor action, their target-based activation, and design of new related drugs)
 RN 118292-36-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

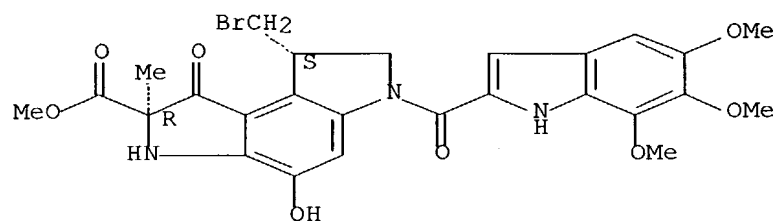
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:157495 CAPLUS Full-text
 DN 136:205412
 TI Oligopeptide-based prodrugs activated by plasmin and their use in cancer chemotherapy
 IN Trouet, Andre; Dubois, Vincent; Passioukov, Alexandre
 PA Coulter Pharmaceutical, Inc., USA
 SO PCT Int. Appl., 67 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002015700	A1	20020228	WO 2001-US26476	20010823
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001086727	A5	20020304	AU 2001-86727	20010823
PRAI	US 2000-227686P	P	20000824		
	WO 2001-US26476	W	20010823		

OS MARPAT 136:205412

AB A prodrug, cleavable by plasmin, comprises a therapeutic agent capable of entering a target cell, e.g., a tumor or inflammatory cell, an oligopeptide having a plasmin peptide substrate of 2-4 amino acids and mono- or di-peptide linkage, a stabilizing group and, optionally, a linker group. Also disclosed are methods of making and using the prodrug compds. For example, the activity of D-Ala-Leu-Lys-Leu-Leu-doxorubicin (I) (preparation given) was evaluated in the B16-B16 murine melanoma model. The mice receiving the prodrug did not show any important weight loss during the experiment and no clin. signs of toxicity were observed. At the same time, the drug had a marked effect on the metastatic growth. At 34.5 $\mu\text{mol/kg}$, I reduced the spread of lung metastases with a decrease of the ratio of the surface occupied by B16-B16 colonies to the non-affected one to $8.2 \pm 1.8\%$ ($P < 0.01$), compared to $45.7 \pm 12.6\%$ and $44.0 \pm 6.3\%$ for non-treated and doxorubicin ($5.2 \mu\text{mol/kg}$)-treated animals. The same prodrug at $69.0 \mu\text{mol/kg}$ provided $1.5 \pm 0.6\%$ of surface affected.

IT 154889-68-6, KW-2189

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (oligopeptide-based prodrugs activated by plasmin for chemotherapy)

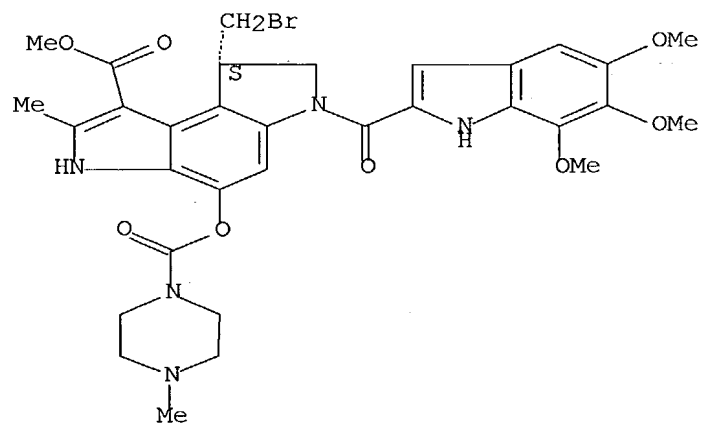
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:10314 CAPLUS Full-text
 DN 136:86054
 TI Tripeptide prodrug compounds
 IN Bebbington, Christopher R.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.
 PA Corixa Corporation, USA
 SO PCT Int. Appl., 102 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002000263	A2	20020103	WO 2001-US40925	20010611
	WO 2002000263	A3	20020815		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1294403	A2	20030326	EP 2001-942249	20010611
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004501875	T2	20040122	JP 2002-505044	20010611
	US 2003181359	A1	20030925	US 2002-311519	20021213
PRAI	US 2000-212880P	P	20000614		
	WO 2001-US40925	W	20010611		

OS CASREACT 136:86054; MARPAT 136:86054

AB The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide AA3-AA2-AA1 (AA1 is leucine, phenylalanine, isoleucine, alanine, glycine, tyrosine, 2-naphthylalanine, or serine; AA2 is alanine, leucine, tyrosine, glycine, serine, 3-pyridylalanine, 2-thienylalanine, aminoisobutyric acid, threonine, or phenylalanine; AA3 is leucine, sarcosine, tyrosine, phenylalanine, p-chloro- or p-nitrophenylalanine, valine, norleucine, norvaline, phenylglycine, tryptophan, tetrahydroisoquinoline-3-carboxylic acid, 3-pyridylalanine, alanine, glycine, 2-thienylalanine, methionine, or proline), a stabilizing group and, optionally, a linker group. The prodrug is cleavable by a trouase enzyme such as Thimet oligopeptidase. Thus, Suc-Leu-Ala-Leu-Dox (Suc = succinic acid residue, Dox = doxorubicin residue), prepared by conjugation of doxorubicin hydrochloride with Fmoc-Leu-Ala-Leu-OH, deprotection, and acylation with succinic anhydride, showed tumor-activated prodrug activity on LNCaP, HT-29 and PC-3 cells of 0.016, 0.052, and 0.075 μ M, resp. Suc-Leu-Ala-Leu-Dox is better tolerated in vivo than is doxorubicin.

IT 154889-68-6, KW 2189

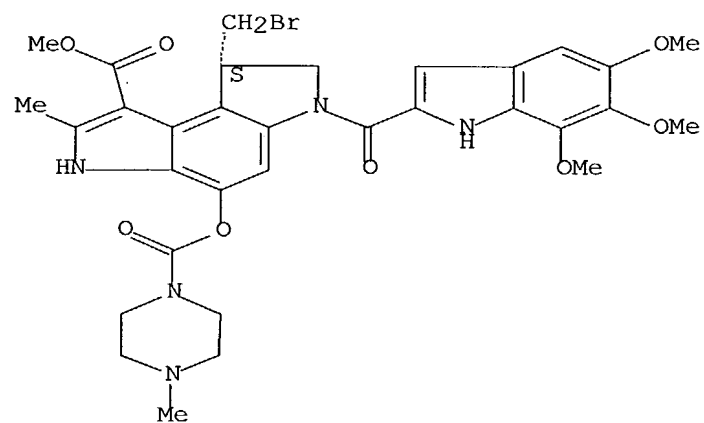
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tripeptide prodrug compds.)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-

trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

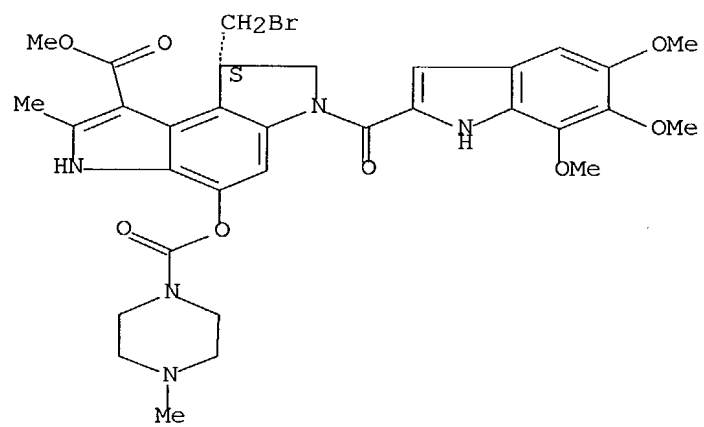
Absolute stereochemistry.



L10 ANSWER 14 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:923644 CAPLUS Full-text
 DN 136:58787
 TI Enzyme-cleavable prodrug compounds
 IN Nieder, Matthew H.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.;
 Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.
 PA Corixa Corporation, USA
 SO PCT Int. Appl., 159 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095945	A2	20011220	WO 2001-US18903	20010611
	WO 2001095945	A3	20020815		
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	EP 1294405	A2	20030326	EP 2001-950291	20010611
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
	JP 2004510703	T2	20040408	JP 2002-510122	20010611
PRAI	US 2000-211887P	P	20000614		
	US 2001-290448P	P	20010511		
	WO 2001-US18903	W	20010611		
OS	MARPAT 136:58787				
AB	The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme, thimet oligopeptidase (TOP). Also disclosed are methods of designing prodrugs by utilizing TOP-cleavage sequences within the conjugate and methods of treating patients with prodrugs of the invention.				
IT	154889-68-6 , KW-2189 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (enzyme-cleavable prodrug compds.)				
RN	154889-68-6 CAPLUS				
CN	Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA				
INDEX	NAME)				

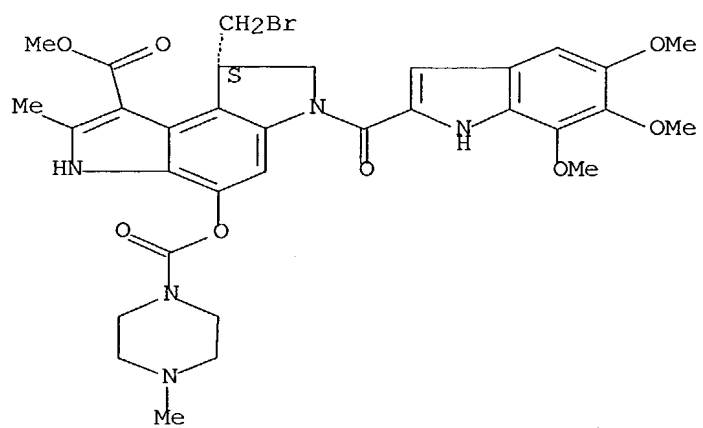
Absolute stereochemistry.



L10 ANSWER 15 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:923642 CAPLUS Full-text
 DN 136:74618
 TI Prodrug compounds with isoleucine
 IN Pickford, Lesley B.; Gangwar, Sanjeev; Lobl, Thomas J.; Nieder, Matthew
 H.; Yarranton, Geoffrey T.
 PA Corixa Corporation, USA
 SO PCT Int. Appl., 107 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095943	A2	20011220	WO 2001-US18857	20010611
	WO 2001095943	A3	20020829		
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
EP	1294404	A2	20030326	EP 2001-944442	20010611
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
	JP 2004510702	T2	20040408	JP 2002-510120	20010611
	US 2004039160	A1	20040226	US 2002-311411	20021213
PRAI	US 2000-211686P	P	20000614		
	WO 2001-US18857	W	20010611		
OS	MARPAT 136:74618				
AB	The compds. of the invention are modified forms of therapeutic agents. A typical prodrug compound of the invention comprises a therapeutic agent, an oligopeptide having an isoleucine residue, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by an enzyme associated with the target cell. Methods of making and using the compds. are also disclosed.				
IT	154889-68-6 , Kw-2189				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prodrug compds. with isoleucine)				
RN	154889-68-6 CAPLUS				
CN	Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA				
INDEX	NAME)				

Absolute stereochemistry.



L10 ANSWER 16 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:479762 CAPLUS Full-text
DN 135:81987
TI Sterilization of hardly water-soluble compounds by filtration
IN Kato, Hiromi; Tashiro, Yoshikazu
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001181207	A2	20010703	JP 1999-369550	19991227
PRAI	JP 1999-369550		19991227		
OS	MARPAT 135:81987				

AB Hardly water-soluble pharmaceutically active agents, especially antitumor DC-89 derivs., are entrapped in liposomes having an average particle size of $\leq 0.2 \mu\text{m}$ and an injectable solution containing the liposomes is sterilizable by filtration.

L10 ANSWER 17 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:315840 CAPLUS Full-text

DN 135:76706

TI Derivatives of Methyl 5-Methyl-4-oxo-1,2,4,5,8,8a-hexahydrocyclopropa[c]-

pyrrolo[3,2-e]indole-7-carboxylate: A Case of Inverse Electronic Effects

on the Reactivity of CC-1065 Derivatives

AU Castedo, Luis; Delamano, Jose; Enjo, Juan; Fernandez, Jesus; Gravalos, Dolores G.; Leis, Ramon; Lopez, Carmen; Marcos, Carlos F.; Rios, Ana; Tojo, Gabriel

CS Departamento de Quimica Organica, Unidad Asociada al CSIC Universidad de Santiago de Compostela, Santiago de Compostela, 15706, Spain

SO Journal of the American Chemical Society (2001), 123(21), 5102-5103
CODEN: JACSAT; ISSN: 0002-7863

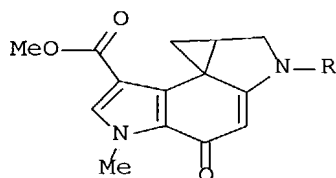
PB American Chemical Society

DT Journal

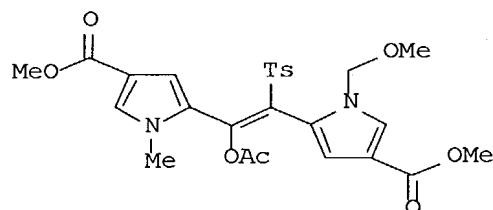
LA English

OS CASREACT 135:76706

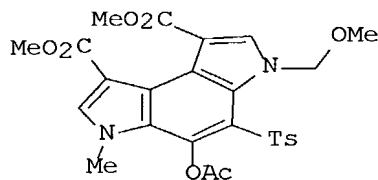
GI



I



II



III

AB A series of Me 5-methyl-4-oxo-1,2,4,8,8a-hexahydrocyclopropa[c]-pyrrolo[3,2-e]indole-7-carboxylate derivs., I (R = H, CONH₂, CO₂C(Me)₃, COMe, or SO₂Me), were prepared. A key reaction was the photochem. oxidative cyclization of bis-pyrrolethene II to produce intermediate III. These novel 5-methyl-cyclopropaindolones were found to exhibit a non-linear solvolytic behavior, with a region of increased reactivity (log k) correlating with decreased electron-deficiency as reflected by the σ_p Hammett constant of their R substituents. Cyclopropaindolones I (R = H, CONH₂, CO₂C(Me)₃, COMe, or SO₂Me) also show an abnormal

relationship between solvolytic reactivity and in vitro cytotoxic potency relative to other CC-1065 analogs, with those compds. with greater potency also having greater solvolytic reactivity.

IT 170431-00-2P 170431-01-3P 170431-02-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

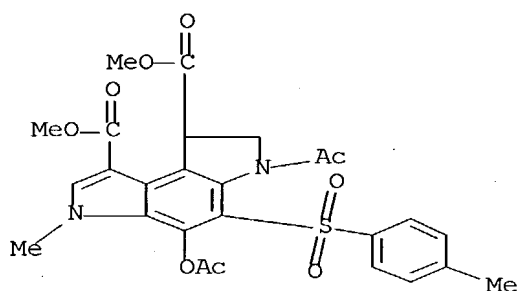
(Reactant or reagent)

(inverse electronic effects on the reactivity of 5-methyl-cyclopropaindolone CC-1065 derivs)

RN 170431-00-2 CAPLUS

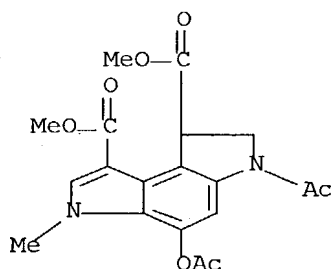
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-
1,2,3,6-tetrahydro-6-methyl-4-[(4-methylphenyl)sulfonyl]-, dimethyl ester

(9CI) (CA INDEX NAME)



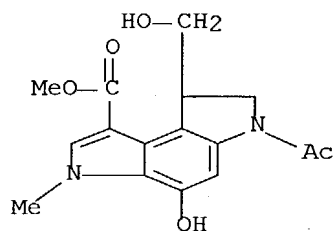
RN 170431-01-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-
1,2,3,6-tetrahydro-6-methyl-, dimethyl ester (9CI) (CA INDEX NAME)



RN 170431-02-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-acetyl-3,6,7,8-tetrahydro-4-hydroxy-8-(hydroxymethyl)-3-methyl-, methyl ester (9CI)
(CA INDEX NAME)

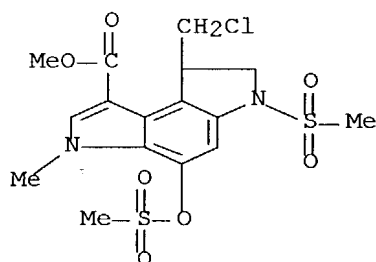


IT 346669-65-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(inverse electronic effects on the reactivity of 5-methyl-
cyclopropaindolone CC-1065 derivs)

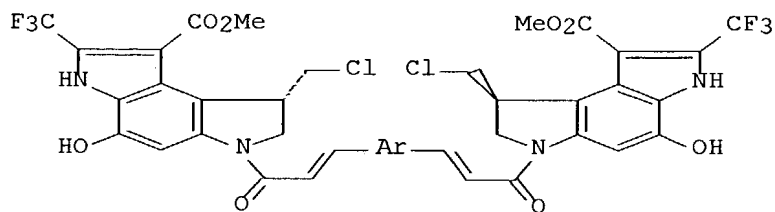
RN 346669-65-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-3-methyl-6-(methylsulfonyl)-4-[(methylsulfonyl)oxy]-, methyl
ester (9CI) (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:214543 CAPLUS Full-text
 DN 135:5544
 TI Novel Seco Cyclopropa[c]pyrrolo[3,2-e]indole Bisalkylators Bearing a
 3,3'-Arylenebisacryloyl Group as a Linker
 AU Fukuda, Yasumichi; Seto, Shigeki; Furuta, Hirosuke; Ebisu, Hiroyuki;
 Oomori, Yasuo; Terashima, Shiro
 CS Central Research Laboratories, Kyorin Pharmaceutical Company Ltd., Nogi
 Tochigi, 329-0114, Japan
 SO Journal of Medicinal Chemistry (2001), 44(9), 1396-1406
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 135:5544
 GI



I

AB Novel seco cyclopropa[c]pyrrolo[3,2-e]indole (CPI) bisalkylators were
 synthesized and evaluated their antitumor activity. Among these
 derivs., I (AT-760) showed more potent cytotoxicity and antitumor
 activity against HeLaS3 human uterine cervix carcinoma cells and colon
 26 adenocarcinoma cells, resp., than bizelesin (U-77,779). It also
 appeared that I exhibits improved in vivo efficacy in the human colon
 CX-1 model when compared to either bizelesin mitomycin C. Efficacious
 doses for I are 2-fold lower than those for bizelesin.

IT **341556-98-7P 341556-99-8P 341557-00-4P**
341557-01-5P 341557-02-6P 341557-03-7P
341557-04-8P 341557-05-9P 341557-06-0P
341557-07-1P 341557-08-2P 341557-09-3P
341557-10-6P 341557-11-7P 341557-12-8P
341557-13-9P 341557-14-0P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation)

(preparation and antitumor activity of
 arylenebis(acryloylpyrroloindoles))

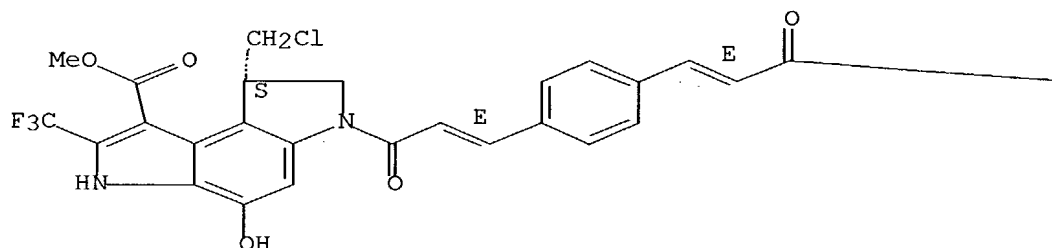
RN 341556-98-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-
 phenylenebis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-
 (9CI)

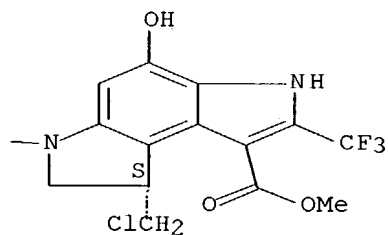
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A

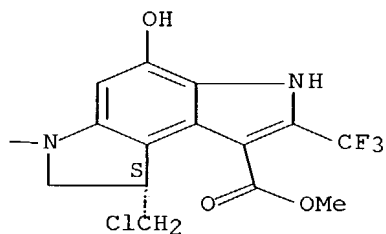
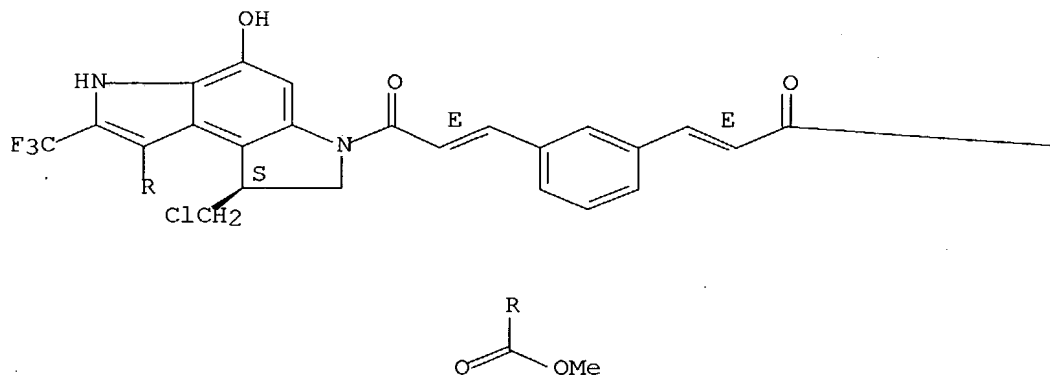


PAGE 1-B



RN 341556-99-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,3-
phenylenebis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



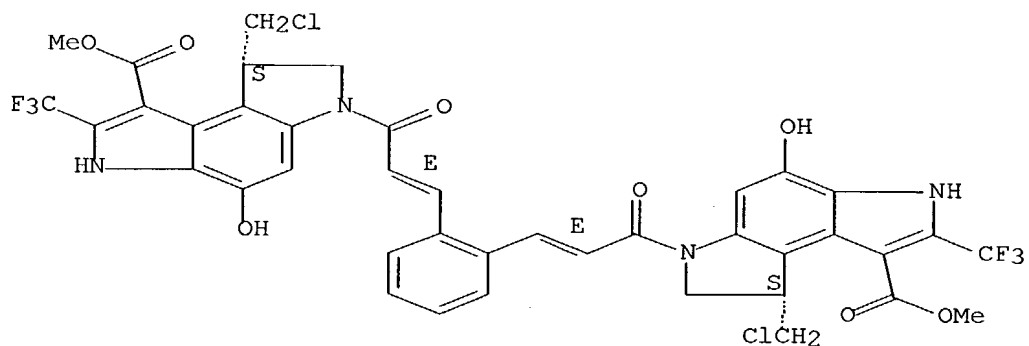
RN 341557-00-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,2-phenylenebis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI)

(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

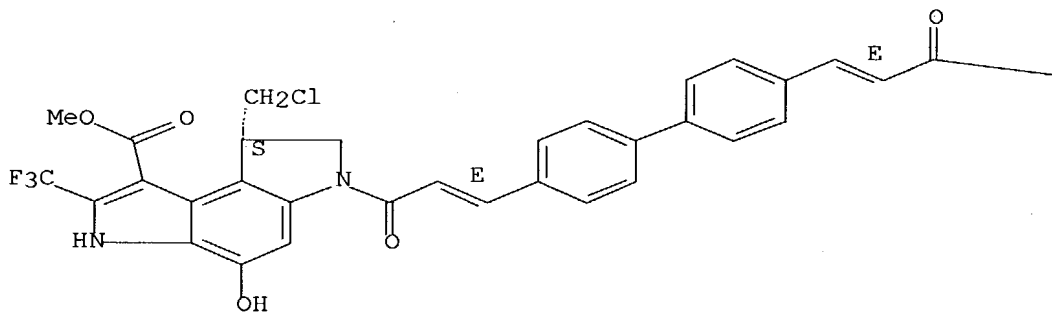
Double bond geometry as shown.

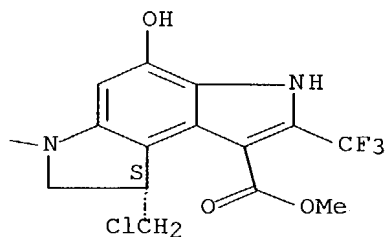


RN 341557-01-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[1,1'-biphenyl]-4,4'-diylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as shown.

PAGE 1-A



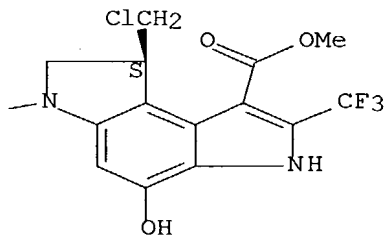
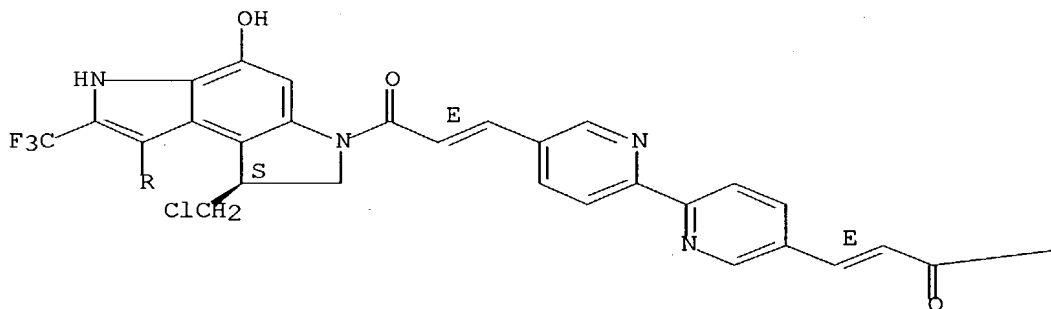


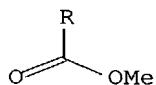
RN 341557-02-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[2,2'-bipyridine]-5,5'-diylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI)

(CA INDEX NAME)

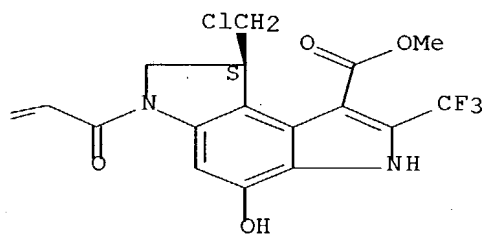
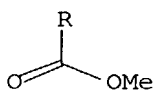
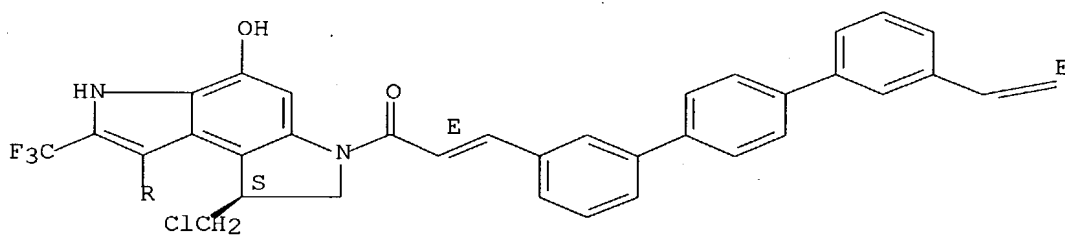
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.





RN 341557-03-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[[1,1':4',1''-terphenyl]-3,3''-diylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI) (CA INDEX NAME)

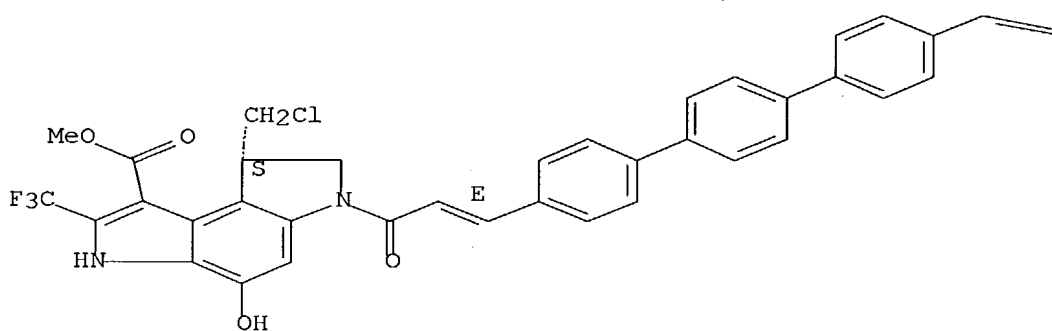
Absolute stereochemistry. Rotation (-).
 Double bond geometry as shown.



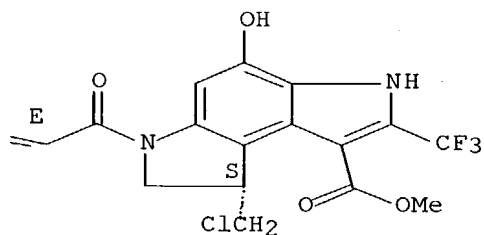
RN 341557-04-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[1,1':4',1''-terphenyl]-4,4''-diylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as shown.

PAGE 1-A



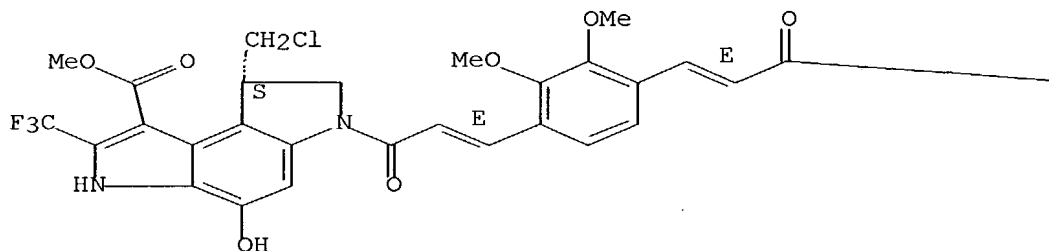
PAGE 1-B



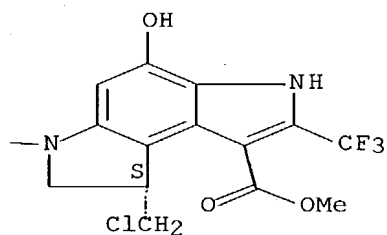
RN 341557-05-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,3-dimethoxy-1,4-phenylene)bis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A

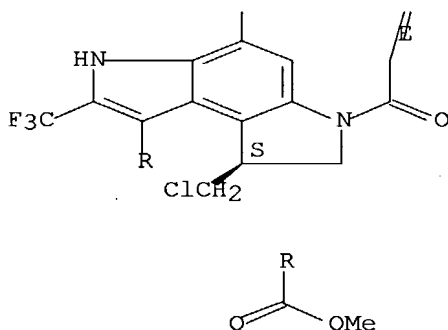
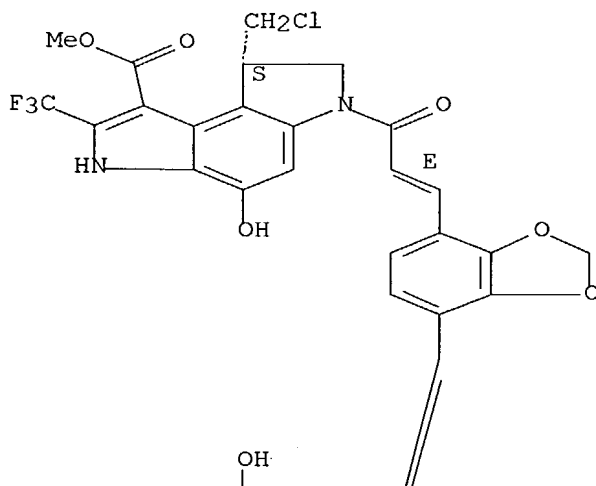


PAGE 1-B



RN 341557-06-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,3-benzodioxole-4,7-diylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

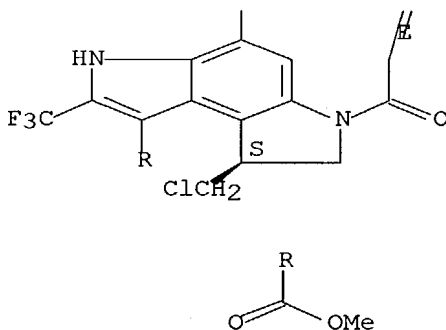
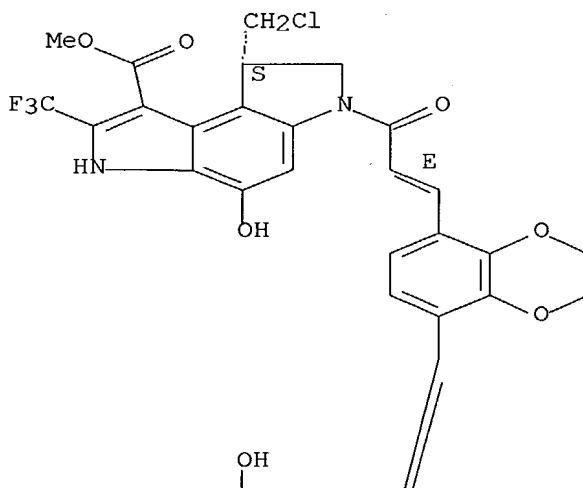


RN 341557-07-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,3-dihydro-1,4-benzodioxin-5,8-diyl)bis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI) (CA INDEX NAME)

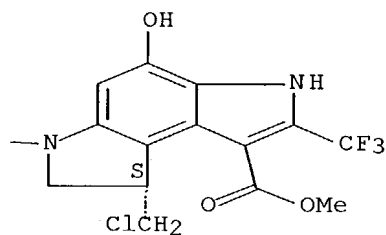
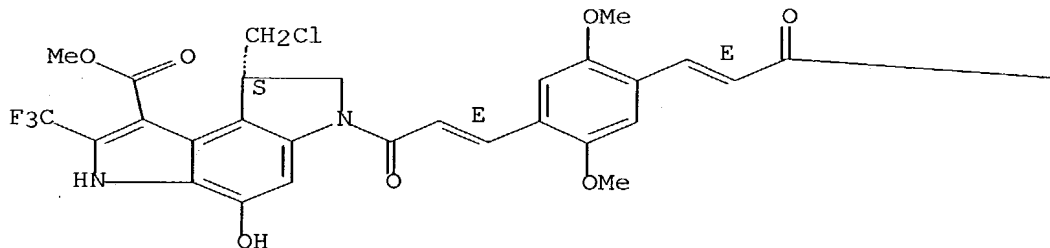
Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



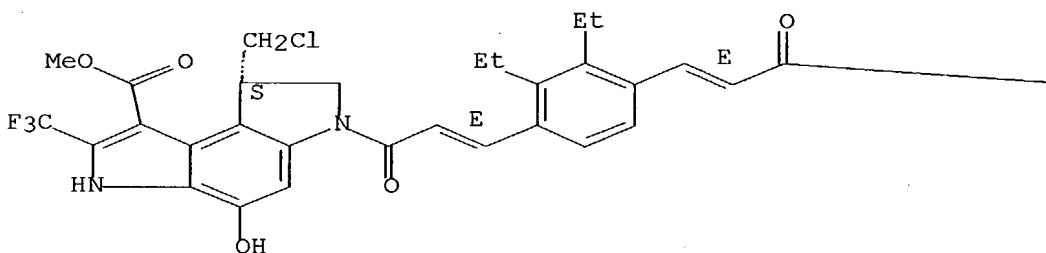
RN 341557-08-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,5-dimethoxy-1,4-phenylene)bis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as shown.

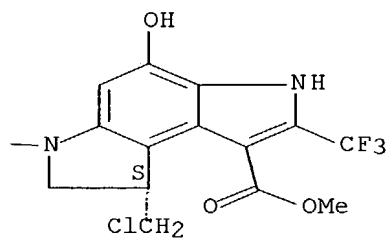


RN 341557-09-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,3-diethyl-1,4-phenylene)bis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry as shown.



PAGE 1-B

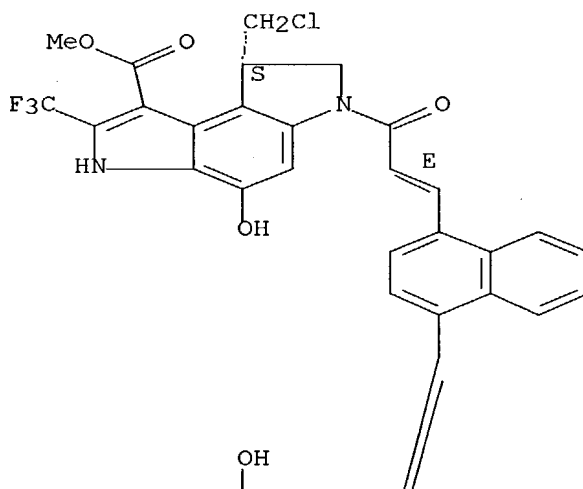


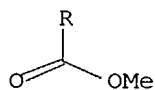
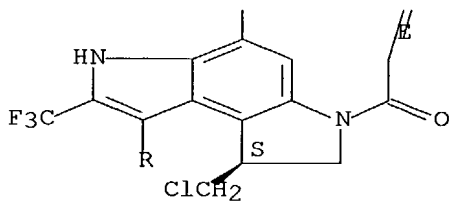
RN 341557-10-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-naphthalenediylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



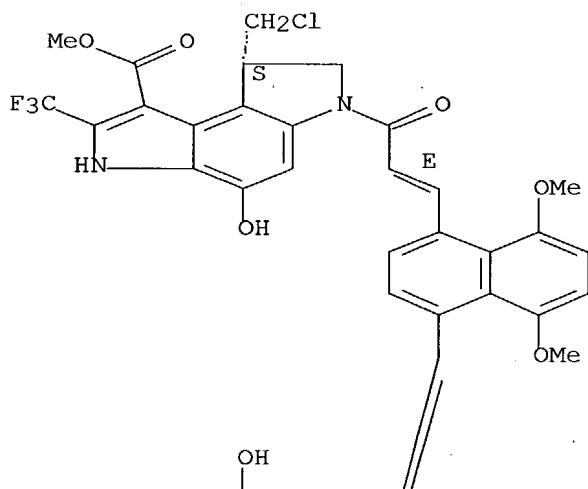


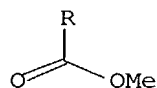
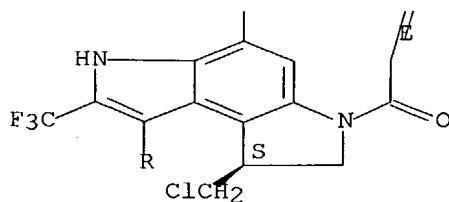
RN 341557-11-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(5,8-dimethoxy-1,4-

naphthalenediyl)bis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

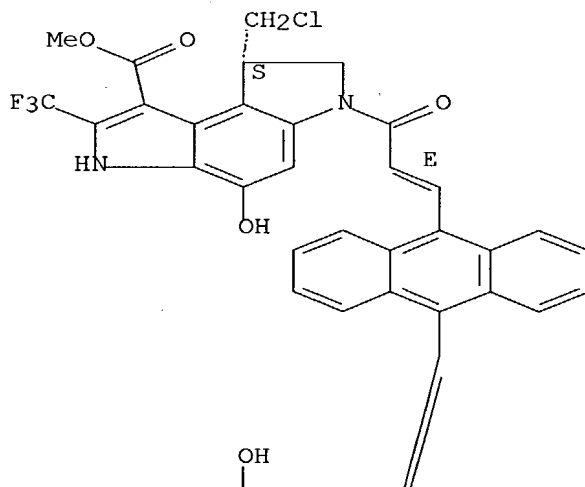


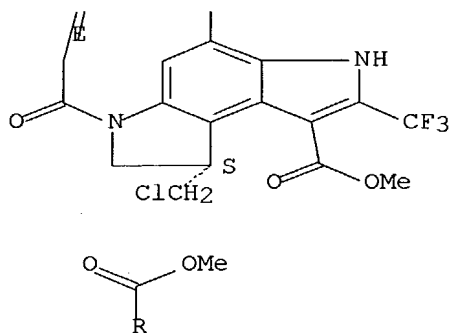


RN 341557-12-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[9,10-anthracenediylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.





RN 341557-14-0 CAPLUS

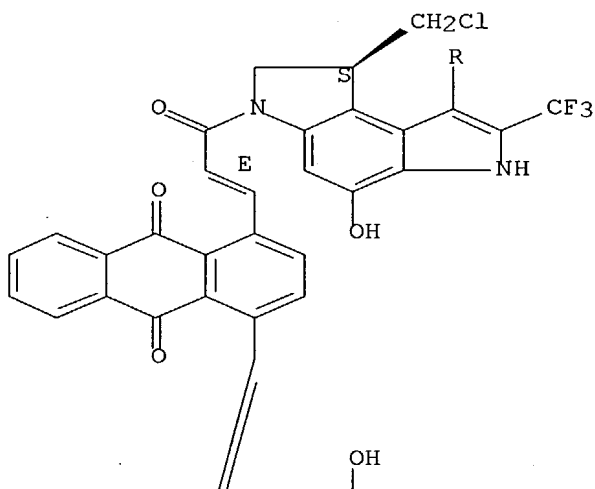
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(9,10-dihydro-9,10-

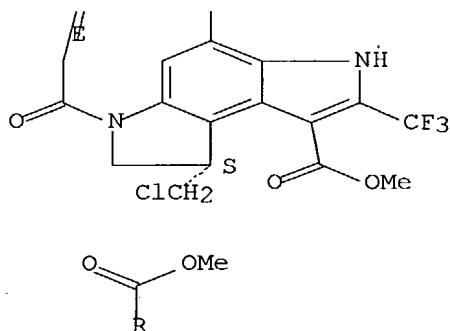
dioxo-1,4-anthracenediyl)]bis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl

ester, (8S,8'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



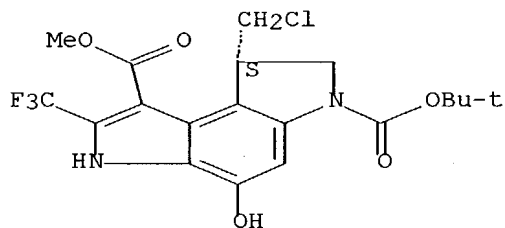
IT **157904-28-4**RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor activity of

arylenebis(acryloylpyrroloindoles))

RN 157904-28-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:488720 CAPLUS Full-text

DN 133:266627

TI Synthesis and antitumor activity of duocarmycin derivatives: A-ring pyrrole compounds bearing β -(5',6',7'-trimethoxy-2'-indolyl)acryloyl group

AU Amishiro, N.; Nagamura, S.; Kobayashi, E.; Okamoto, A.; Gomi, K.; Okabe, M.; Saito, H.

CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Shizuoka, 411-8731, Japan

SO Bioorganic & Medicinal Chemistry (2000), 8(7), 1637-1643
CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

AB A series of A-ring pyrrole derivs. of duocarmycin bearing the β -(5',6',7'-trimethoxy-2'-indolyl)acryloyl group were synthesized, and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. New Seg-B analogs bearing the β -(5',6',7'-trimethoxy-2'-indolyl)acryloyl group containing a double bond as a spacer had lower peripheral blood toxicity than the derivs. bearing the 5',6',7'-trimethoxyindole-2'-carboxyl group in Seg-B of the natural type. Moreover, most of them exhibited potent antitumor activity against in vivo murine tumor models.

IT 154889-68-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (preparation and antitumor activity of duocarmycin derivs.)

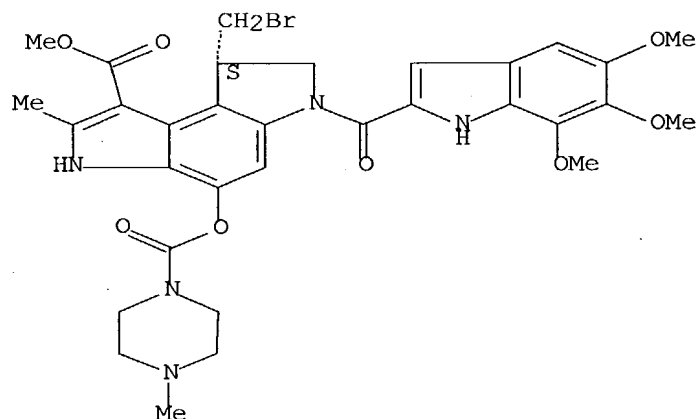
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



IT 297137-23-6P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); PRP (Properties); SPN (Synthetic preparation);
BIOL

(Biological study); PREP (Preparation)
(preparation and antitumor activity of duocarmycin derivs.)

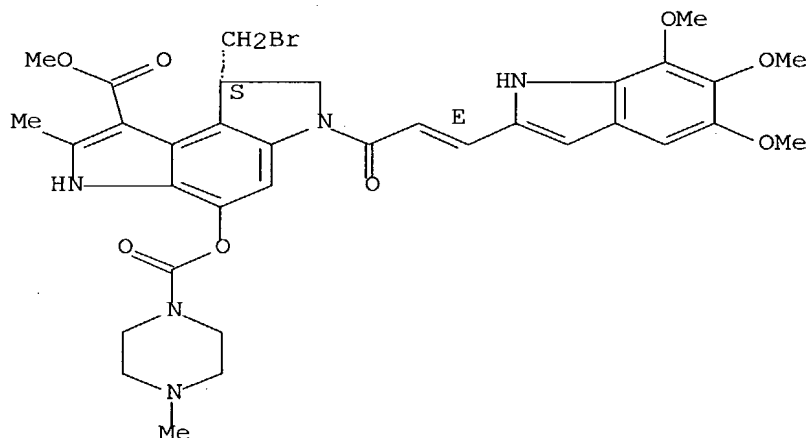
RN 297137-23-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(2E)-3-
(5,6,7-trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester,
monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

● HBr

IT 205051-48-5P 297137-24-7P 297137-25-8P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(preparation and antitumor activity of duocarmycin derivs.)

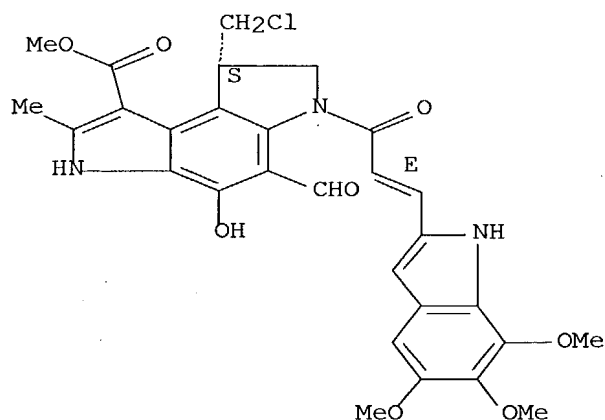
RN 205051-48-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-5-
formyl-
3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(2E)-1-oxo-3-(5,6,7-trimethoxy-
1H-

indol-2-yl)-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 297137-24-7 CAPLUS

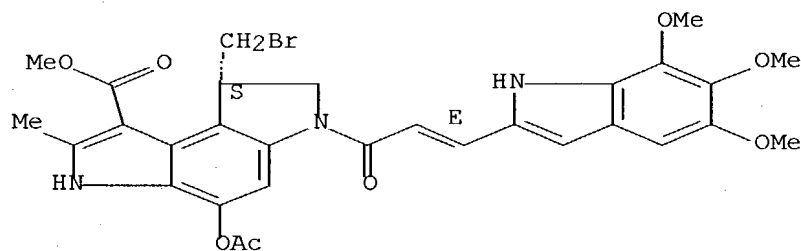
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(2E)-3-(5,6,7-trimethoxy-

1H-

indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



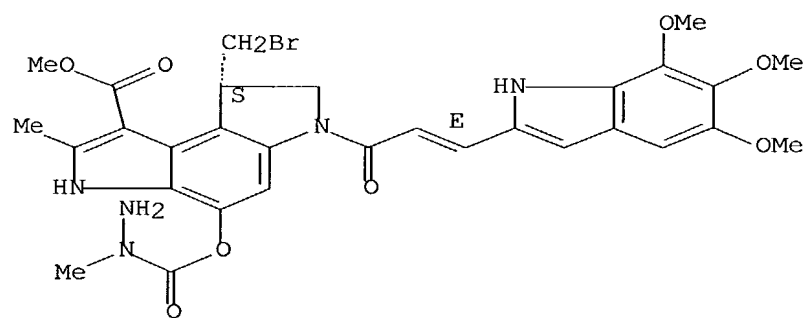
RN 297137-25-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methylhydrazino)carbonyl]oxy]-6-[(2E)-3-(5,6,7-

trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:488717 CAPLUS Full-text
DN 133:281632
TI Design, synthesis and cytotoxicity evaluation of 1-chloromethyl-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) dimers
AU Jia, G.; Lown, J. W.
CS Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2, Can.
SO Bioorganic & Medicinal Chemistry (2000), 8(7), 1607-1617
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
GI

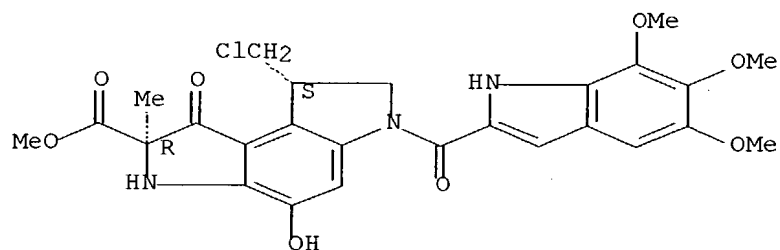
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Three types of 1-chloromethyl-5-hydroxy-1,2-dihydro-3H-benz[e]indole (seco-CBI) dimers were designed, synthesized and evaluated in vitro by NCI against nine types of cancer cells. Biol. results showed that the antitumor activities of these seco-CBI dimers were strongly related to the position and length of the linker and generally with potency increasing in the order of C7-C7 dimers [I; X1 = (CH2)_n, n = 3 - 6] < C7-N3 dimers [II; X2 = (CH2)_n, n = 3 - 6] < N3-N3 dimers [III; X3 = (CH2)_n, n = 3 - 6]. Compound II [X2 = (CH2)₆] showed significant activity against CCRT-CEM, HL-60 (TB), MOLT-4, and SR leukemia cell lines and the MCF 7 breast cancer cell line with GI50 values < 0.01 μM. N3-N3 dimer III [X3 = (CH2)₃] displayed striking potency against leukemia, CNS cancer, melanoma and prostate cancer cell lines with GI50 values < 0.01 μM against all the cell lines and showed the highest overall potency of the agents examined (GMG = 0.0120 μM).

IT **118292-36-7DP**, Duocarmycin C2, dimer analogs **124325-94-6DP**, Duocarmycin B2, dimer analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (design, synthesis and cytotoxicity evaluation of seco-CBI dimers)

RN 118292-36-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

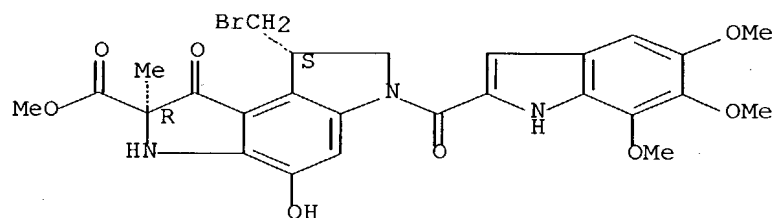
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

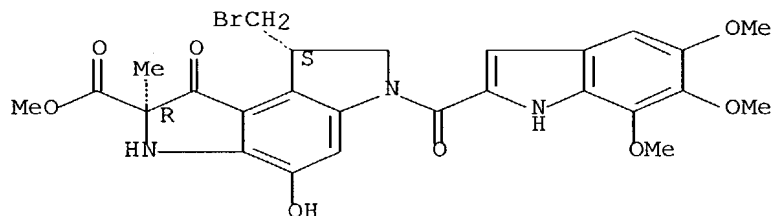
Absolute stereochemistry.



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:424475 CAPLUS Full-text
 DN 133:26526
 TI A phase II pilot study of KW-2189 in patients with advanced renal cell carcinoma
 AU Small, Eric J.; Figlin, Robert; Petrylak, Daniel; Vaughn, David J.; Sartor, Oliver; Horak, Ivan; Pincus, Rosemarie; Kremer, Alton; Bowden, Chris
 CS UCSF Comprehensive Cancer Center, University of California, San Francisco, CA, USA
 SO Investigational New Drugs (2000), 18(2), 193-197
 CODEN: INNDDK; ISSN: 0167-6997
 PB Kluwer Academic Publishers
 DT Journal
 LA English
 AB KW-2189 is a semi-synthetic, water-soluble analog of duocarmycin B2, a new class of potent antitumor antibiotics produced by streptomyces, with improved in vitro antitumor potency. Forty patients with pathol. confirmed metastatic renal cell carcinoma were treated in this multicenter, open-label phase II trial. All patients received 0.4 mg/m2 KW-2189 as an IV infusion for Cycle 1. Cycles were repeated every 5 to 6 wk with escalations to 0.5 mg/m2 in the absence of significant toxicity or disease progression. No patient had an objective response. The most common drug-related toxicity was hematol.-delayed neutropenia and thrombocytopenia, with recovery by week 6. Non-hematol. toxicity consisted of mild to moderate fatigue, nausea and vomiting, and anorexia that was generally manageable. KW-2189 in this dose and schedule has a predictable safety profile of reversible myelosuppression. No activity in metastatic renal cell carcinoma was demonstrated.
 IT **124325-94-6D**, Duocarmycin B2, analog **154889-68-6**, KW-2189
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phase II pilot study of KW-2189 in patients with advanced renal cell carcinoma)
 RN 124325-94-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



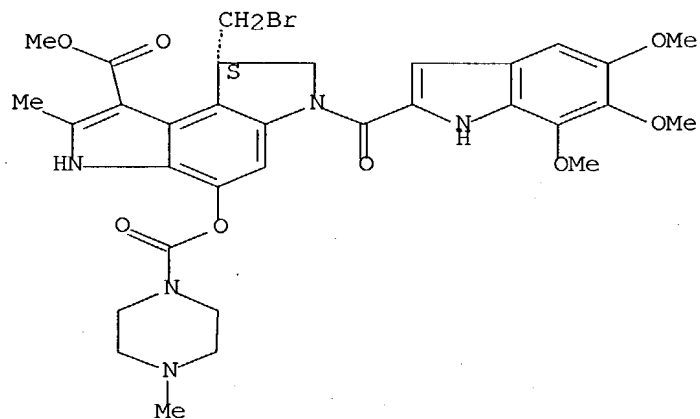
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[{(4-methyl-1-piperazinyl)carbonyl}oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:401690 CAPLUS Full-text

DN 133:48878

TI Oligopeptide prodrug compounds and process for preparation thereof

IN Lobl, Thomas J.; Dubois, Vincent; Fernandez, Anne-Marie; Gangwar, Sanjeev;

Lewis, Evan; Nieder, Matthew H.; Trouet, Andre; Viski, Peter; Yarranton, Geoffrey T.

PA Coulter Pharmaceutical, Inc., USA

SO PCT Int. Appl., 125 pp.

CODEN: PIXXD2

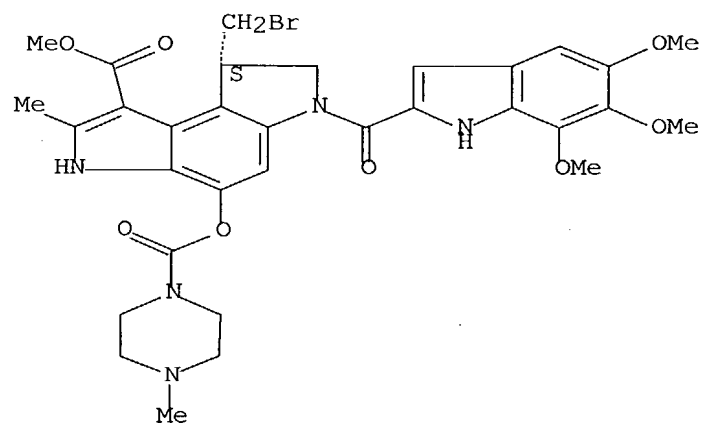
DT Patent

LA English

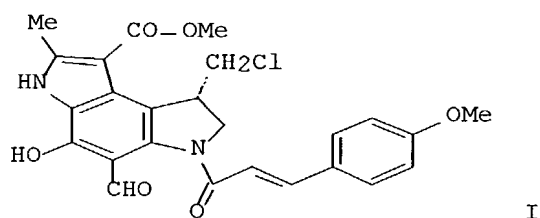
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000033888	A2	20000615	WO 1999-US30393	19991210
	WO 2000033888	A3	20011108		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1144011	A2	20011017	EP 1999-967462	19991210
	EP 1144011	A3	20020206		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2003518000	T2	20030603	JP 2000-586378	19991210
	US 2002142955	A1	20021003	US 2001-879442	20010611
PRAI	US 1998-111793P	P	19981211		
	US 1999-119312P	P	19990208		
	WO 1999-US30393	W	19991210		
	US 2000-211887P	P	20000614		
	US 2001-290448P	P	20010511		
OS	MARPAT 133:48878				
AB	The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme trouase. Also disclosed are processes for making the prodrug compds.				
IT	154889-68-6 , KW-2189				
	RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (oligopeptide prodrug compds. and process for preparation thereof)				
RN	154889-68-6 CAPLUS				
CN	Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA				
INDEX	NAME)				

Absolute stereochemistry.

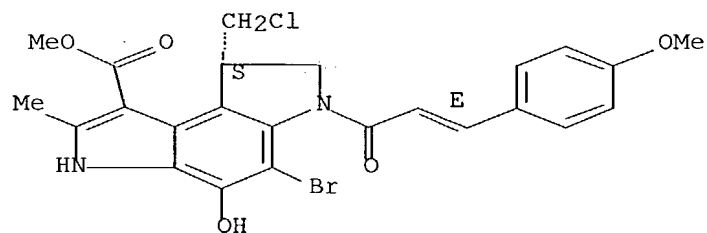


L10 ANSWER 23 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:395947 CAPLUS Full-text
 DN 133:150386
 TI Synthesis and antitumor activity of duocarmycin derivatives:
 modification
 at the C-7 position of segment-A of A-ring pyrrole compounds
 AU Amishiro, N.; Okamoto, A.; Okabe, M.; Saito, H.
 CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd.,
 Nagaizumi, Sunto, Shizuoka, 411-8731, Japan
 SO Bioorganic & Medicinal Chemistry (2000), 8(5), 1195-1201
 CODEN: BMECEP; ISSN: 0968-0896
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 GI



AB A series of the C7-substituted A-ring pyrrole derivs. of duocarmycin
 were synthesized, and evaluated for in vitro anticellular activity
 against HeLa S3 cells and in vivo antitumor activity against murine
 sarcoma 180 in mice. All of the C7-substituted A-ring pyrrole compds.
 decreased potency in vitro and in vivo. However, some showed strong
 antitumor activity with T/C values less than 0.3. Among them, the 7-
 formyl compound I showed remarkable potent in vivo antitumor activity
 and low peripheral blood toxicity.
 IT **205051-26-9P**
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
 (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis and antitumor activity of C7-substituted A-ring pyrrole
 duocarmycin derivs.)
 RN 205051-26-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 5-bromo-8-
 (chloromethyl)-
 3,6,7,8-tetrahydro-4-hydroxy-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-
 propenyl]-
 2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



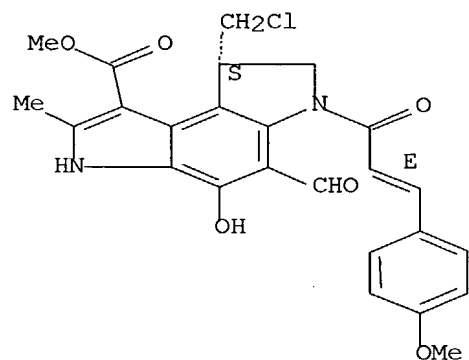
IT 205051-32-7P 205051-34-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of C7-substituted A-ring pyrrole duocarmycin derivs.)

RN 205051-32-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-5-formyl-3,6,7,8-tetrahydro-4-hydroxy-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, (8S)- (9CI) (CA INDEX NAME)

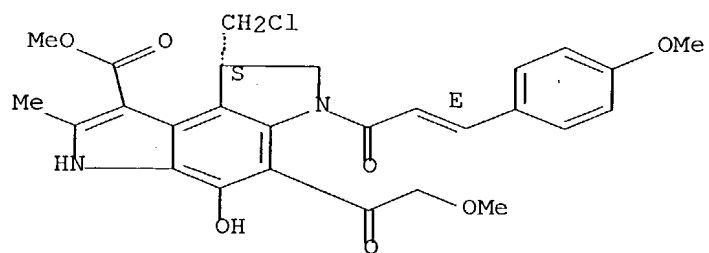
Absolute stereochemistry.
Double bond geometry as shown.



RN 205051-34-9 CAPLUS

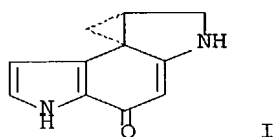
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-5-(methoxyacetyl)-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 24 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:301528 CAPLUS Full-text
 DN 133:58647
 TI Synthesis and Evaluation of 1,2,8,8a-Tetrahydrocyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, the Parent Alkylation Subunit of CC-1065 and the Duocarmycins: Impact of the Alkylation Subunit Substituents and Its Implications for DNA Alkylation Catalysis
 AU Boger, Dale L.; Santillan, Alejandro, Jr.; Searcey, Mark; Brunette, Steven
 R.; Wolkenberg, Scott E.; Hedrick, Michael P.; Jin, Qing
 CS Department of Chemistry and The Skaggs Institute for Chemical Biology,
 The Scripps Research Institute, La Jolla, CA, 92037, USA
 SO Journal of Organic Chemistry (2000), 65(13), 4101-4111
 CODEN: JOCEAH; ISSN: 0022-3263
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 133:58647
 GI



AB Synthesis of 1,2,8,8a-tetrahydrocyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one (I), the parent CC-1065 and duocarmycin SA alkylation subunit, is detailed. The parent CPI alkylation subunit lacks the C7 Me substituent of the CC-1065 alkylation subunit and the C6 methoxycarbonyl group of duocarmycin SA, and their examination permitted the establishment of the impact of these natural product substituents. The studies revealed a CPI stability comparable to the CC-1065 alkylation subunit but which was 6+ more reactive than the (+)-duocarmycin SA alkylation subunit, and it displayed the inherent reaction regioselectivity (4:1) of the natural products. The single-crystal X-ray structure of (+)-N-BOC-CPI depicts a near identical stereoelectronic alignment of the cyclopropane accounting for the identical reaction regioselectivity and a slightly diminished vinylogous amide conjugation relative to (+)-N-BOC-DSA suggesting that the stability distinctions stem in part from this difference in the vinylogous amide as well as alterations in the electronic nature of the fused pyrrole. Establishment of the DNA binding properties revealed that the CPI-based agents retain the identical DNA alkylation selectivities of the natural products. More importantly, the C6 methoxycarbonyl group of duocarmycin SA was found to increase the rate (12-13+) and efficiency (10+) of DNA alkylation despite its intrinsic lower reactivity while the CC-1065 C7 Me group was found to slow the DNA alkylation rate (4+) and lower the alkylation efficiency (ca. 4+). The greater DNA alkylation rate and efficiency for duocarmycin SA and related analogs containing the C6 methoxycarbonyl is proposed to be

derived from the extended length that the rigid C6 methoxycarbonyl provides and the resulting increase in the DNA binding-induced conformational change which serves to deconjugate the vinylogous amide and activate the alkylation subunit for nucleophilic attack. The diminished properties resulting from the CC-1065 C7 Me group may be attributed to the steric impediment this substituent introduces to DNA minor groove binding and alkylation. Consistent with this behavior, the duocarmycin SA C6 methoxycarbonyl group increases biol. potency while the CC-1065 C7 Me group diminishes it.

IT 277317-35-8P

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

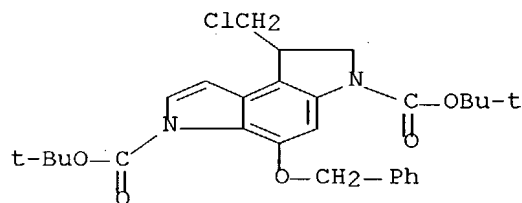
(synthesis and evaluation of tetrahydrocyclopropapyrroloindolones the parent alkylation subunit of CC-1065 and the duocarmycins)

RN 277317-35-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester (9CI) (CA

INDEX

NAME)



IT 277317-90-5P 277317-92-7P

RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(synthesis and evaluation of tetrahydrocyclopropapyrroloindolones the parent alkylation subunit of CC-1065 and the duocarmycins)

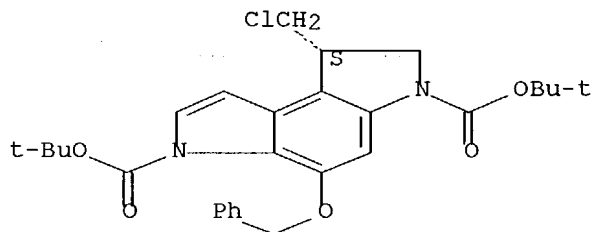
RN 277317-90-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester, (1S)- (9CI)

(CA

INDEX NAME)

Absolute stereochemistry. Rotation (-).



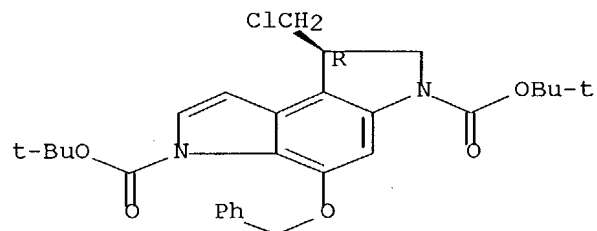
RN 277317-92-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester, (1R)- (9CI)

(CA

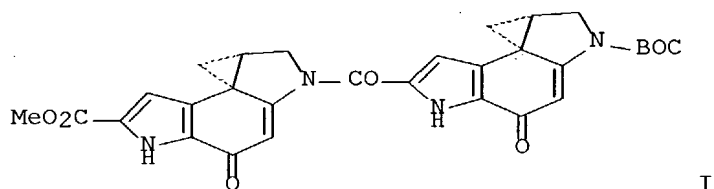
INDEX NAME)

Absolute stereochemistry. Rotation (+).



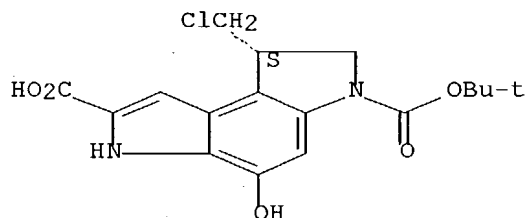
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 25 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:208762 CAPLUS Full-text
 DN 133:30602
 TI Bifunctional alkylating agents derived from duocarmycin SA: potent
 antitumor activity with altered sequence selectivity
 AU Boger, Dale L.; Searcey, Mark; Tse, Winston C.; Jin, Qing
 CS Department of Chemistry and The Skaggs Institute for Chemical Biology,
 The Scripps Research Institute, La Jolla, CA, 92037, USA
 SO Bioorganic & Medicinal Chemistry Letters (2000), 10(5), 495-498
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 OS CASREACT 133:30602
 GI



AB A series of four dimers e.g. I derived from head to tail coupling of the
 two enantiomers of the duocarmycin SA alkylation subunit are described,
 and their bioactivity was discussed.
 IT **190322-73-7P 273410-42-7P 273410-43-8P**
273410-44-9P 273410-45-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT
 (Reactant or reagent)
 (prepn of bifunctional alkylating agents derived from duocarmycin SA:
 potent antitumor activity with altered sequence selectivity)
 RN 190322-73-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) ester,
 (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

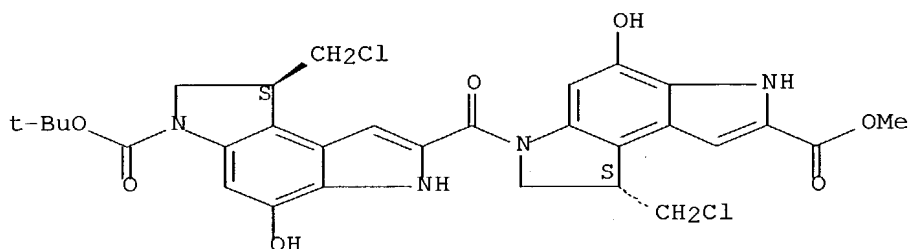


RN 273410-42-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-6-
[[(8S)-

8-(chloromethyl)-6-[(1,1-dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-4-
hydroxybenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydro-4-
hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

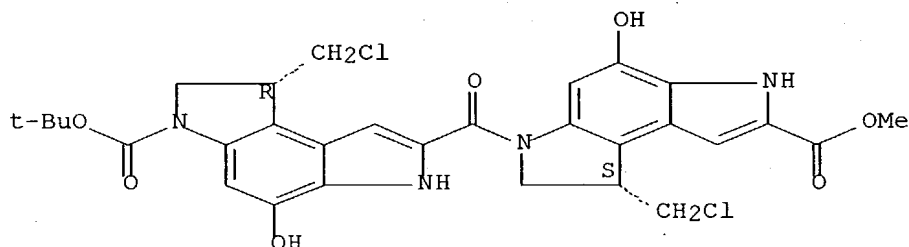


RN 273410-43-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-6-
[[(8R)-

8-(chloromethyl)-6-[(1,1-dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-4-
hydroxybenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydro-4-
hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

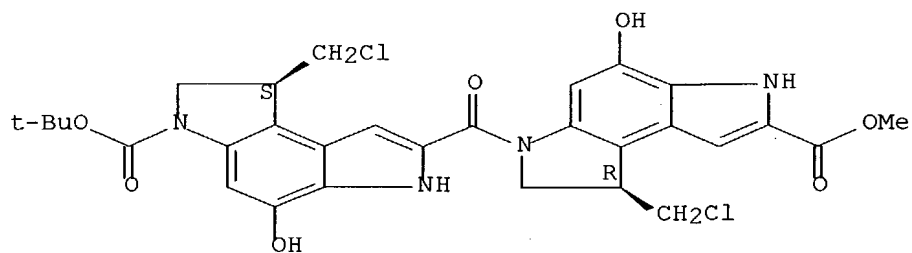


RN 273410-44-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-6-
[[(8S)-

8-(chloromethyl)-6-[(1,1-dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-4-
hydroxybenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydro-4-
hydroxy-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

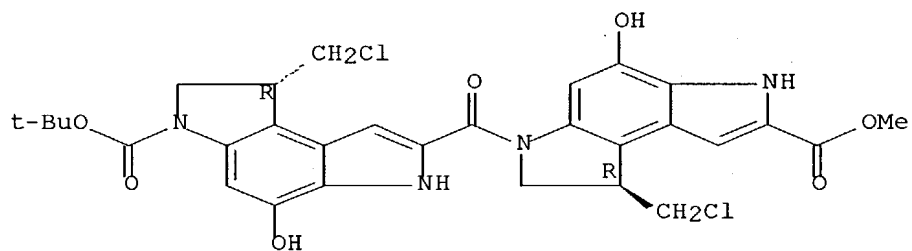


RN 273410-45-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-6-
 [[(8R) -

8-(chloromethyl)-6-[(1,1-dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-4-
 hydroxybenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydro-4-
 hydroxy-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

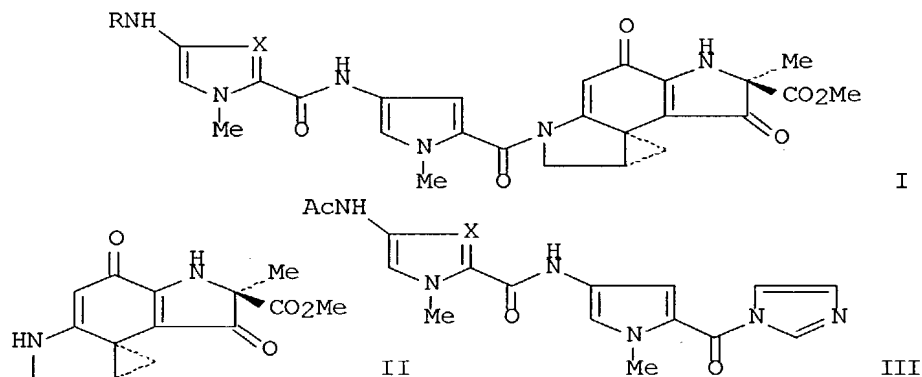
Absolute stereochemistry.



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 26 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2000:191088 CAPLUS Full-text
 DN 132:222536
 TI Preparation of duocarmycin-related compounds alkylating specific base
 sequence of DNA
 IN Sugiyama, Hiroshi; Tao, Zhi Fu; Saito, Isao
 PA Japan Science and Technology Corp., Japan
 SO PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015641	A1	20000323	WO 1999-JP1228	19990312
	W: JP, US				
	JP 2000159768	A2	20000613	JP 1998-260710	19980914
	JP 3045706	B1	20000529		
	JP 3045706	B2	20000529		
	US 6566336	B1	20030520	US 2000-486336	20000530
PRAI	JP 1998-260710	A	19980914		
	WO 1999-JP1228	W	19990312		
OS	MARPAT 132:222536				
GI					



AB The title compds. (I; R = lower acyl, polyamide; X = N, CH), capable of recognizing a minor group in a hydrogen bond of base pairs are prepared Also claimed are alkylating agents for alkylating genes which contain the above compds. and covalently binding to a base, are prepared These compds. recognize a specific base sequence and strongly bind to the adjacent base via a covalent bond and alkylate adenine or guanine base through alkylation mechanism similar to that of duocarmycin A, thus regulating the expression of a gene carrying the above base sequence, and are useful for the prevention or treatment of diseases induced by genes, e.g. cancer genes. Thus, an intermediate (II), which was prepared by treatment of duocarmycin B2 with NaOMe in MeOH and MeCN, was

treated NaH in DMF at -40° to -20° for 2.5 h and then condensed with active amide (III; X = H, CH) (preparation given) at -50° to -30° for 3 h to give I (R = MeCO; X = N, CH) which were tested for alkylating DNA octamers.

IT 124325-94-6, Duocarmycin B2

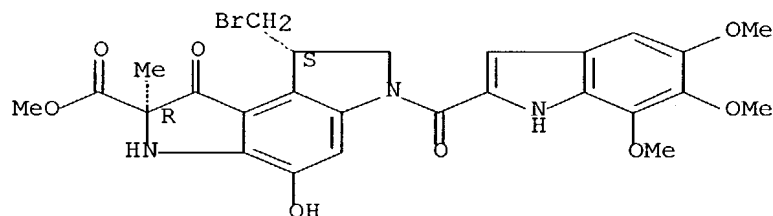
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of duocarmycin-related compds. alkylating specific base sequence of DNA in cancer genes)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

110 ANSWER 27 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:141730 CAPLUS Full-text

DN 132:334367

TI Synthesis and antitumor activity of duocarmycin derivatives:
modification

at C-8 position of A-ring pyrrole compounds bearing the simplified
DNA-binding groups

AU Amishiro, N.; Nagamura, S.; Murakata, C.; Okamoto, A.; Kobayashi, E.;
Asada, M.; Gomi, K.; Tamaoki, T.; Okabe, M.; Yamaguchi, N.; Yamaguchi,
K.;

Saito, H.

CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd.,
Nagaizumi, Sunto, Shizuoka, Japan

SO Bioorganic & Medicinal Chemistry (2000), 8(2), 381-391.
CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

OS CASREACT 132:334367

AB A series of the 8-O-substituted A-ring pyrrole derivs. of duocarmycin
bearing the simplified DNA-binding moieties such as cinnamoyl or
heteroaryl-acryloyl groups were synthesized, and evaluated for in vitro
anticellular activity against HeLa S3 cells and in vivo antitumor
activity against murine sarcoma 180 in mice. In addition, the stability
of the 8-O-substituted analogs in aqueous solution and the conversion to
their active form (cyclopropane compound) from the 8-O-substituted
analogs in mice or human serum were examined. The 8-O-substituted A-ring
pyrrole derivs. bearing the simplified DNA-binding moieties showed
remarkably potent in vivo antitumor activity and low peripheral blood
toxicity compared with the 8-O-substituted A-ring pyrrole derivs. having
the trimethoxyindole skeleton in segment-B (Seg-B), which were equal to
8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates and
4'-methoxy- β -heteroarylacrylates. Moreover, among 8-O-substituted
analogs, several compds. can be chemical or enzymically converted to
their active form in human serum. This result indicated that new 8-O-
substituted derivs. were different prodrugs from KW-2189 and 8-O-
substituted analogs being the same type of prodrug as KW-2189.

IT 160819-28-3 186760-06-5

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); BIOL (Biological study)

(synthesis and antitumor activity of duocarmycin derivs. modified at
C-8 position of A-ring pyrrole compds. bearing the simplified
DNA-binding groups)

RN 160819-28-3 CAPLUS

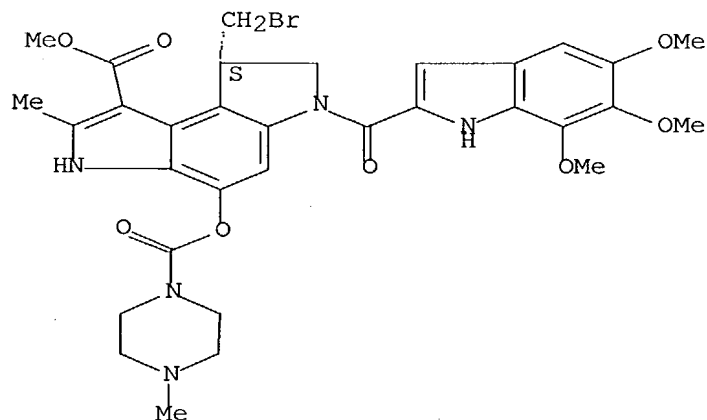
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,

(8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

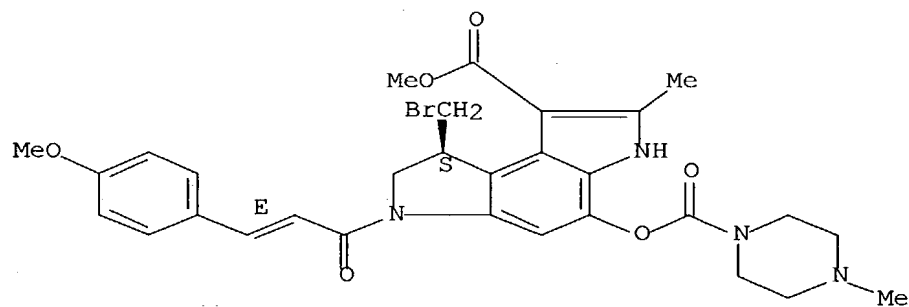


PAGE 2-A

● HBr

RN 186760-06-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● HCl

IT 267899-52-5P
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

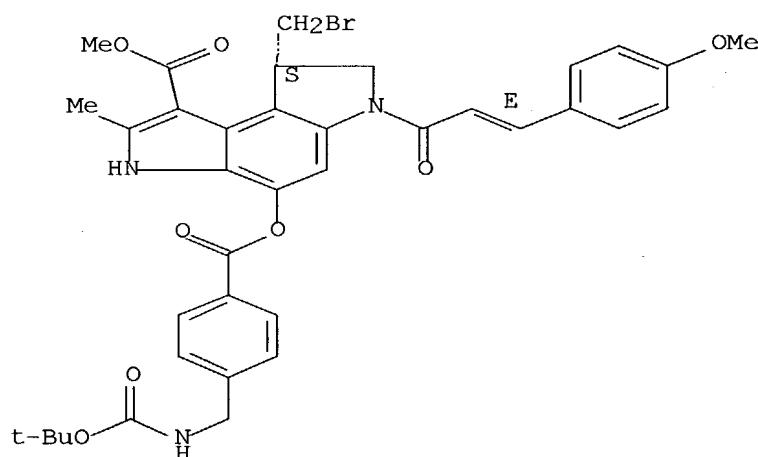
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (synthesis and antitumor activity of duocarmycin derivs. modified at C-8 position of A-ring pyrrole compds. bearing the simplified DNA-binding groups)

RN 267899-52-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]benzoyl]oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 267899-40-1P 267899-41-2P 267899-42-3P
267899-43-4P 267899-44-5P 267899-45-6P
267899-46-7P 267899-47-8P 267899-48-9P
267899-49-0P 267899-50-3P 267899-51-4P
267899-53-6P 267899-54-7P 267899-55-8P
267899-56-9P 267899-57-0P 267899-58-1P
267899-59-2P 267899-60-5P 267899-61-6P
267899-62-7P 267899-64-9P 267899-65-0P
267899-66-1P 267899-67-2P 267899-68-3P
267899-69-4P 267899-70-7P 267899-71-8P
267899-72-9P 267899-73-0P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

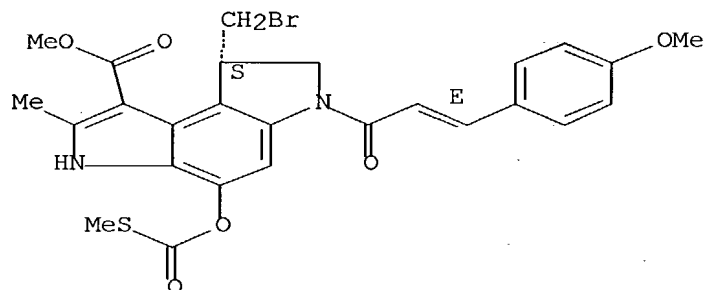
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and antitumor activity of duocarmycin derivs. modified at C-8 position of A-ring pyrrole compds. bearing the simplified DNA-binding groups)

RN 267899-40-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(methylthio)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

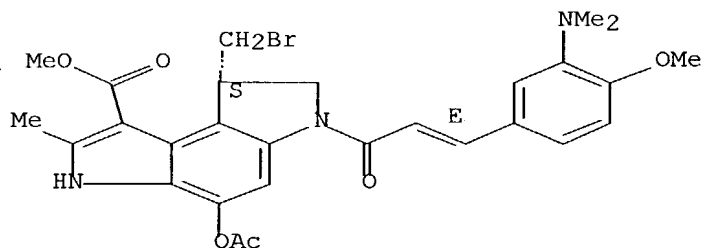
Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-41-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

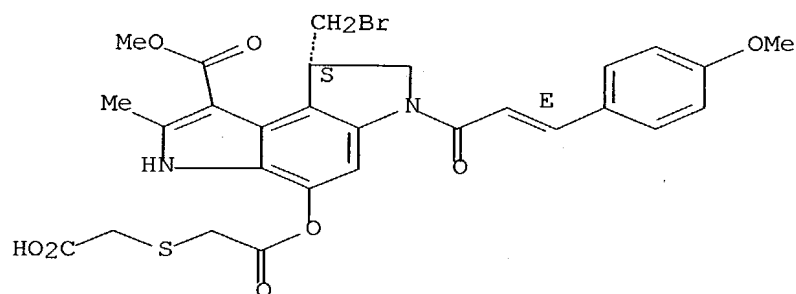
Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-42-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

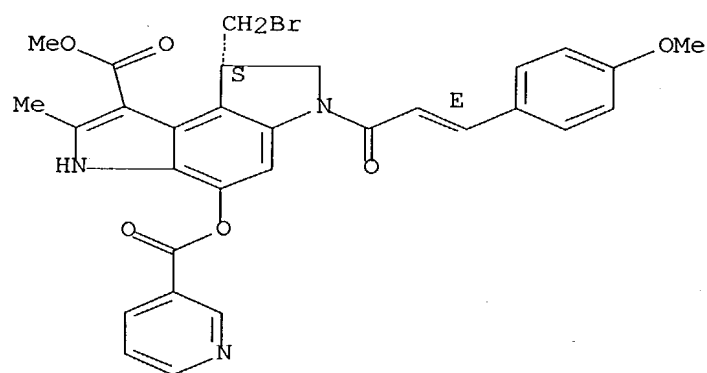


RN 267899-43-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

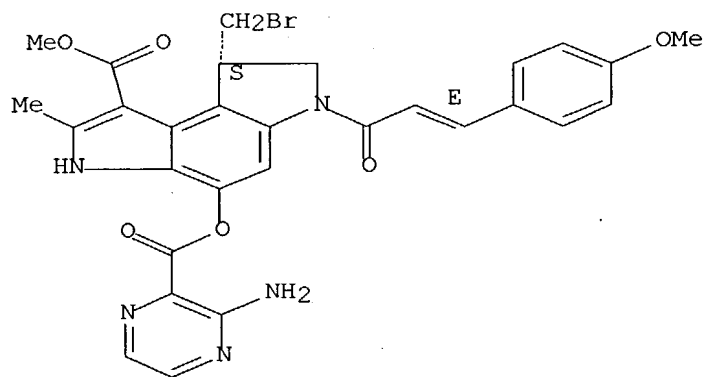


RN 267899-44-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[(3-aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

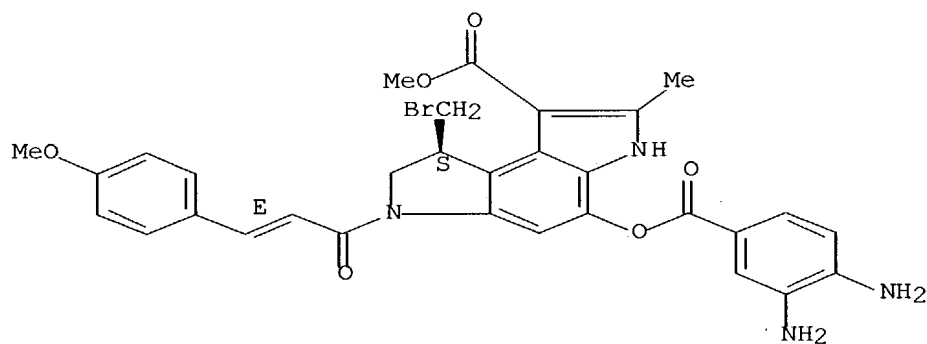
Double bond geometry as shown.



RN 267899-45-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[(3,4-diaminobenzoyl)oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

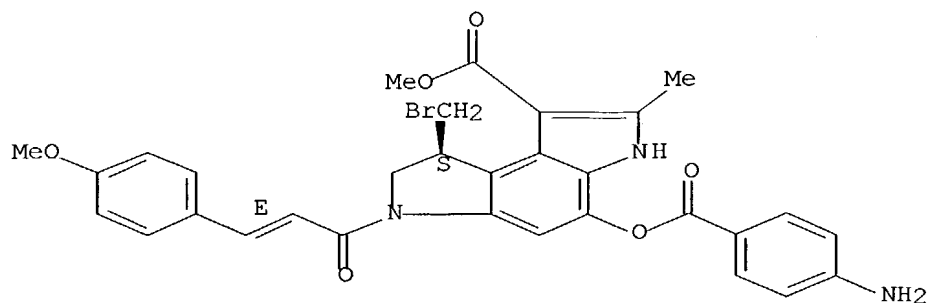
Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-46-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[(4-aminobenzoyl)oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

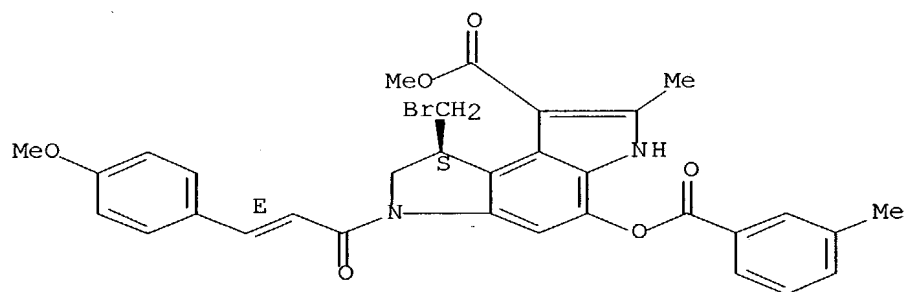


RN 267899-47-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-methylbenzoyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



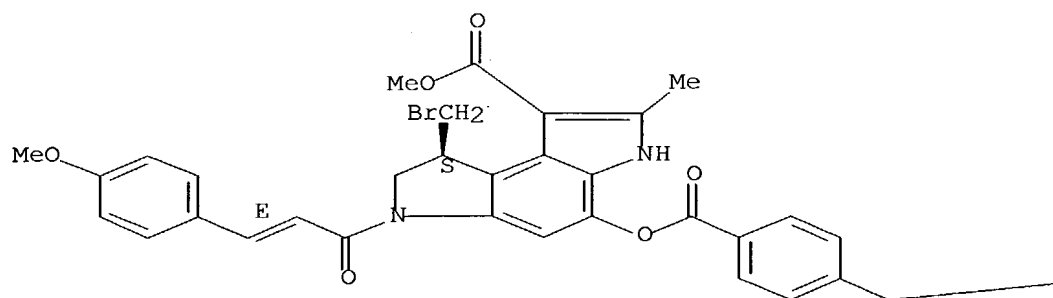
RN 267899-48-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

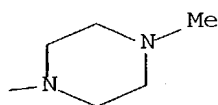
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



RN 267899-49-0 CAPLUS

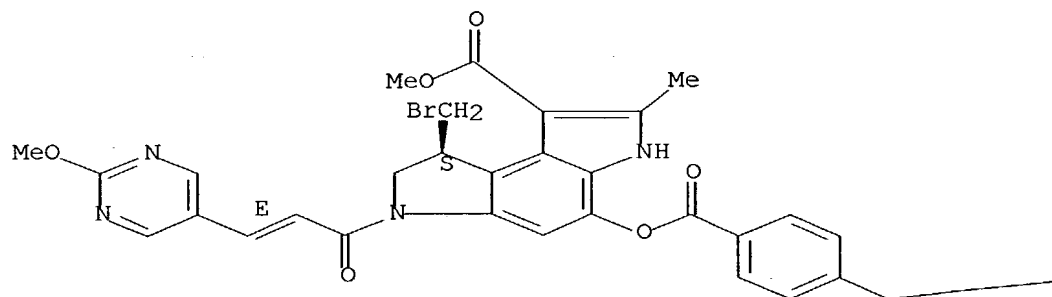
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-

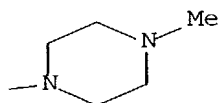
4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

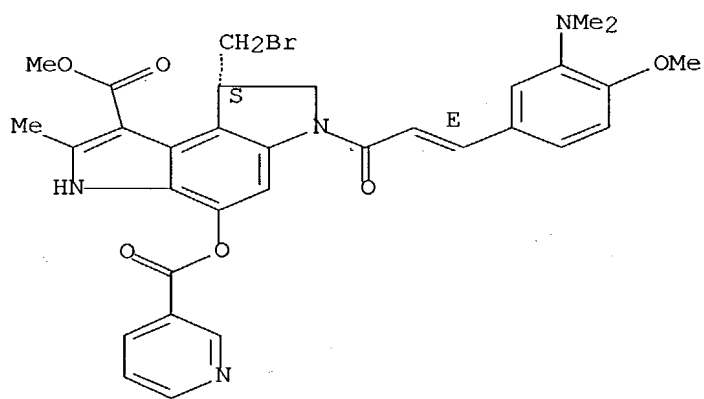
PAGE 1-A





RN 267899-50-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

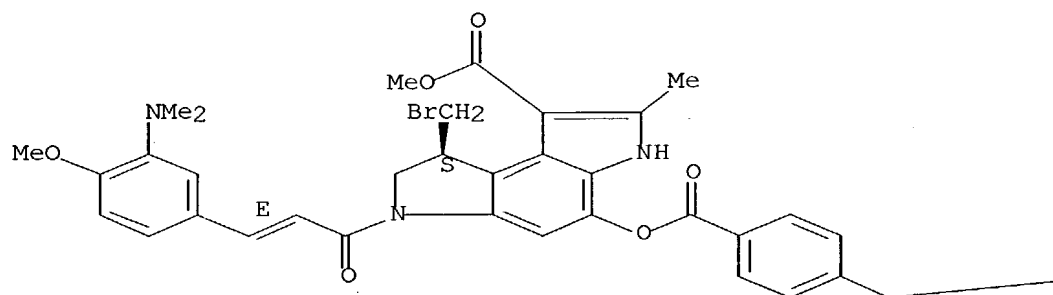


RN 267899-51-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-

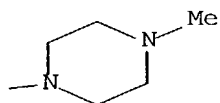
methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

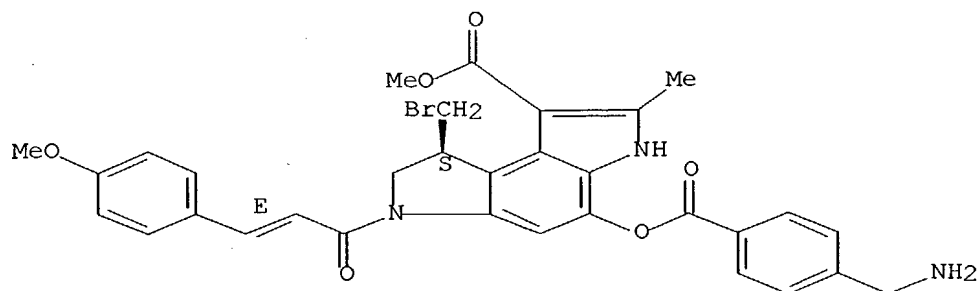


PAGE 1-B



RN 267899-53-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

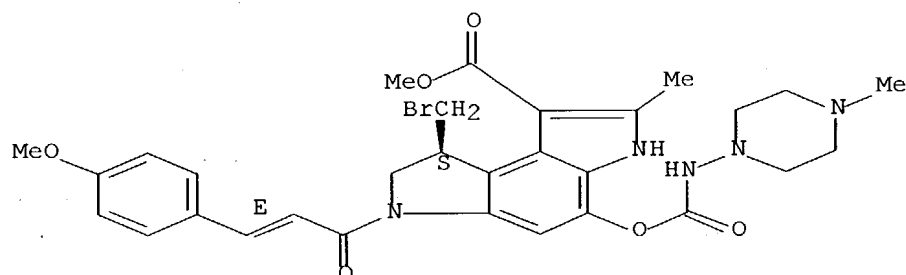


RN 267899-54-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (8S)- (9CI)

(CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

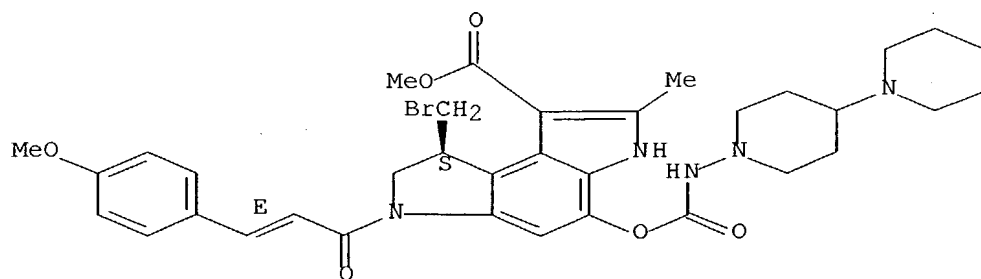


RN 267899-55-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-ylamino]carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI)

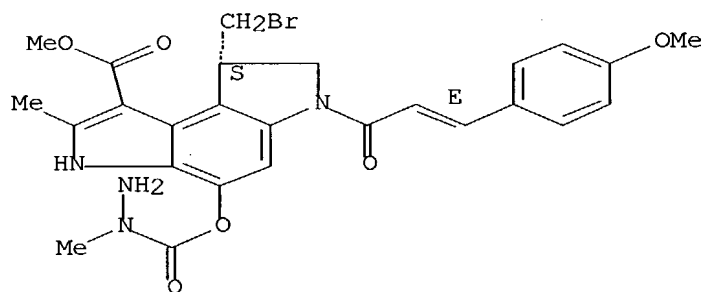
(CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



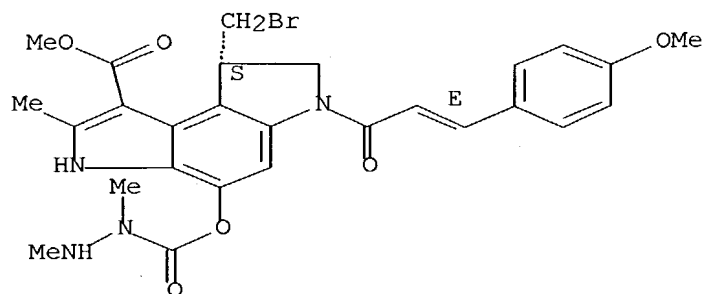
RN 267899-56-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[1-methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 267899-57-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[1,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



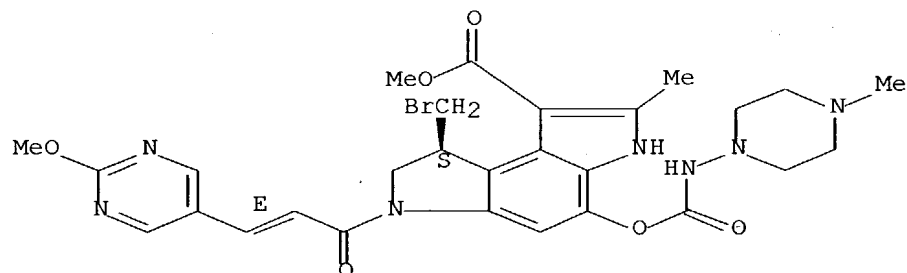
RN 267899-58-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-

4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 267899-59-2 CAPLUS

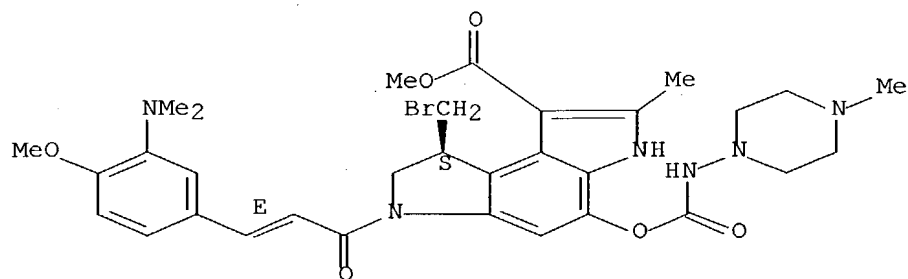
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-

methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

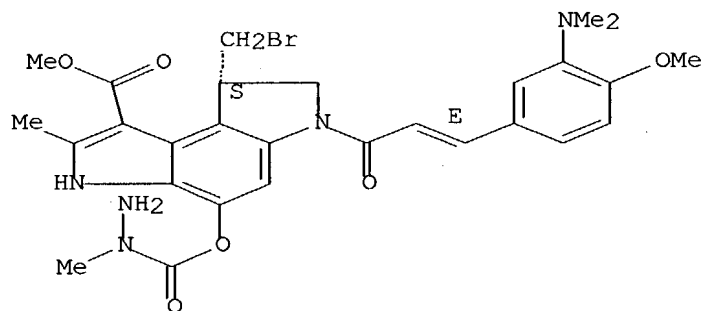
Absolute stereochemistry.

Double bond geometry as shown.



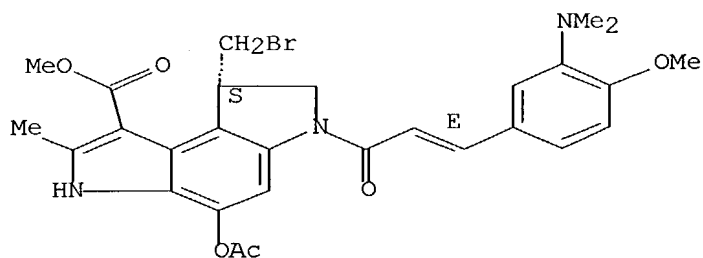
RN 267899-60-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)-(9CI)
 (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 267899-61-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrochloride, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



● HCl

RN - 267899-62-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, monohydrochloride, (8S)- (9CI)

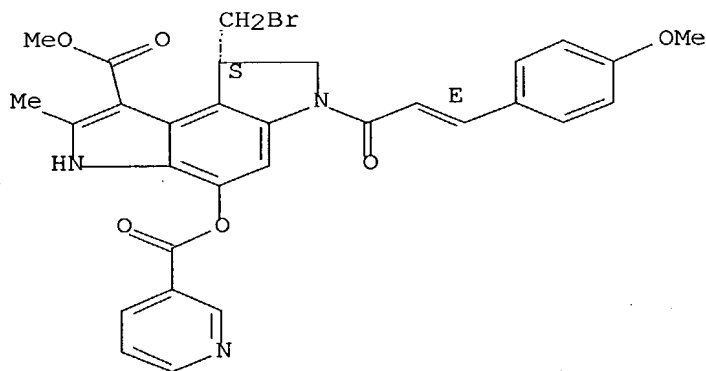
(CA

INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

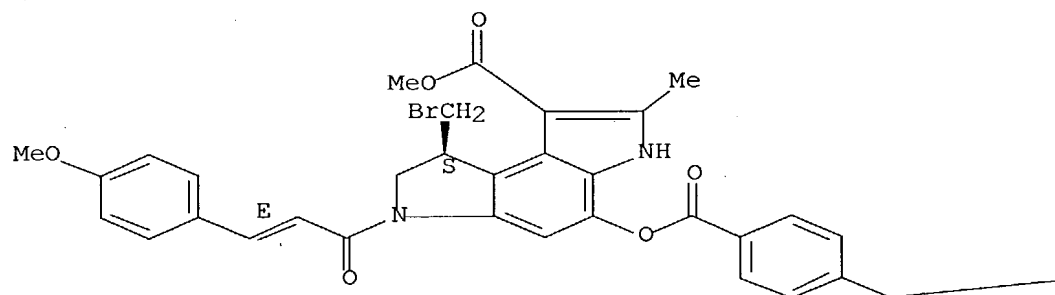
● HCl

RN 267899-64-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

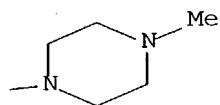
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



● HBr

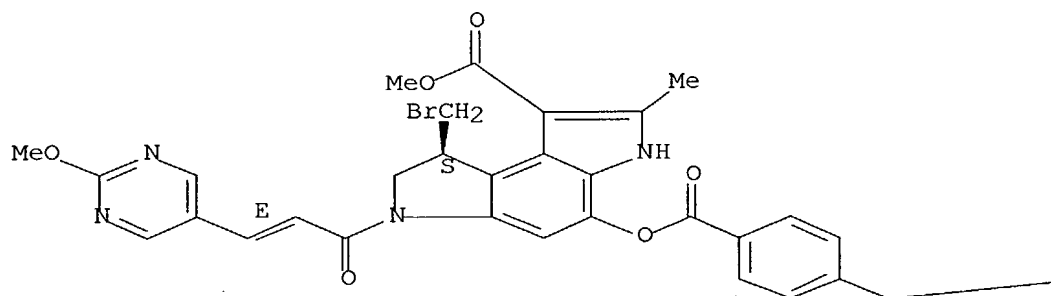
PAGE 1-B



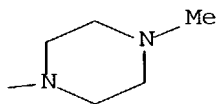
RN 267899-65-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



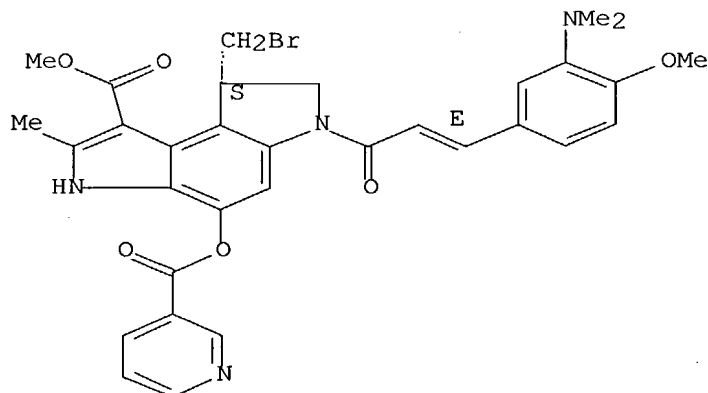
●2 HBr



RN 267899-66-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-
 3-
 [3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-
 tetrahydro-2-
 methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, dihydrobromide,
 (8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



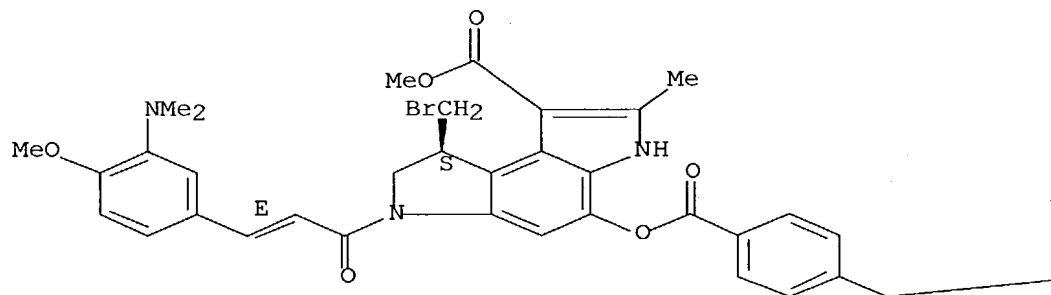
PAGE 2-A

●2 HBr

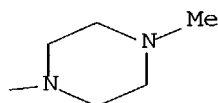
RN 267899-67-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



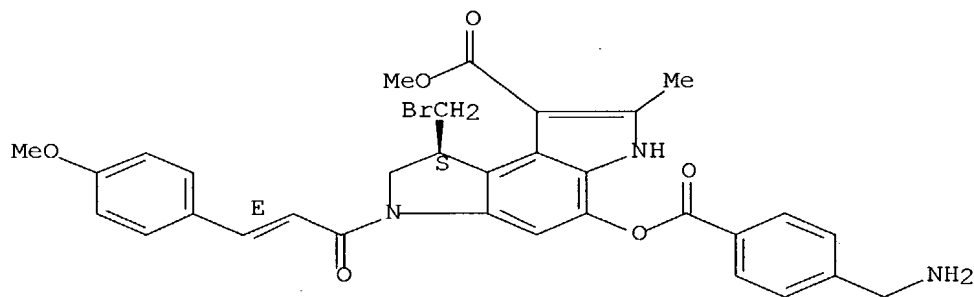
●2 HBr



RN 267899-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

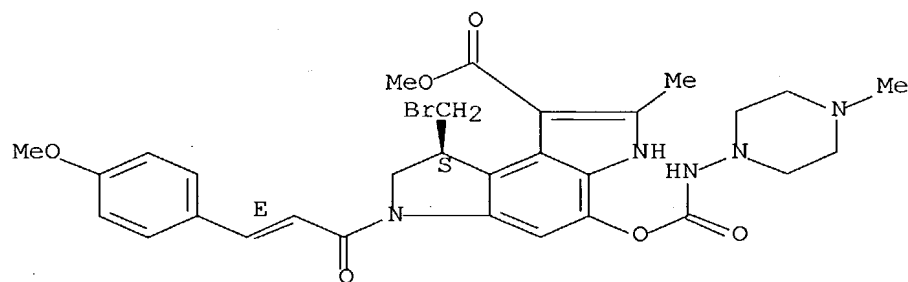


● HBr

RN 267899-69-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

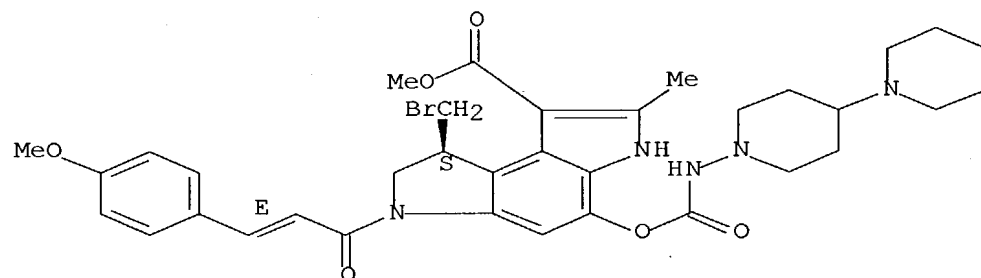
Absolute stereochemistry.
Double bond geometry as shown.



●2 HBr

RN 267899-70-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-ylamino)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

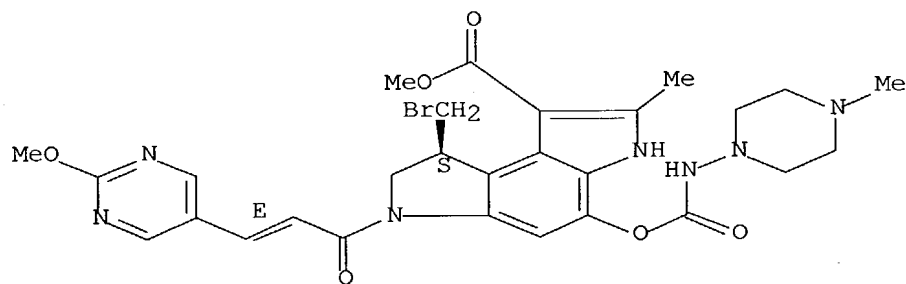
Absolute stereochemistry.
 Double bond geometry as shown.



●2 HBr

RN 267899-71-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

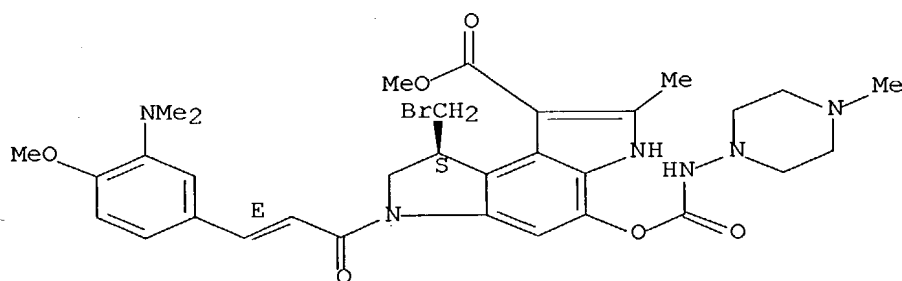
Absolute stereochemistry.
 Double bond geometry as shown.



● HBr

RN 267899-72-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

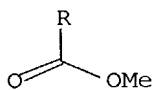
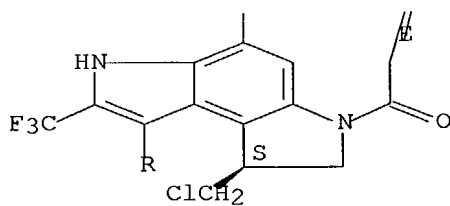
Absolute stereochemistry.
 Double bond geometry as shown.



● HBr

RN 267899-73-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

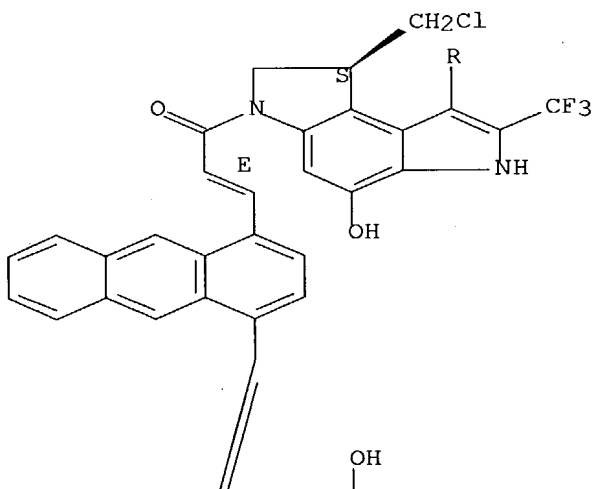
Absolute stereochemistry.
 Double bond geometry as shown.

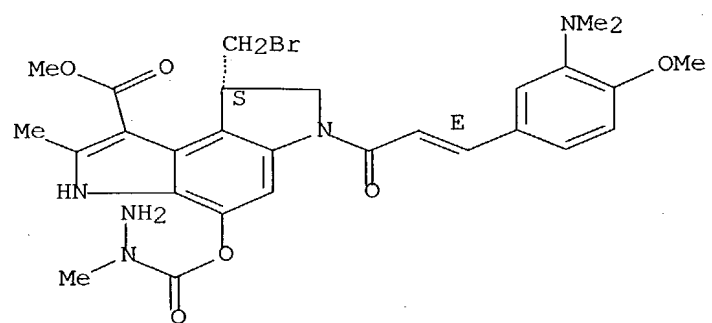


RN 341557-13-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-anthracenediylbis[(2E)-1-oxo-2-propene-3,1-diyl]]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.





L10 ANSWER 28 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:716681 CAPLUS Full-text

DN 132:49819

TI Synthesis and antitumor activity of water-soluble duocarmycin B1 prodrugs

AU Asai, Akira; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu

CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, Machida, 194-8533, Japan

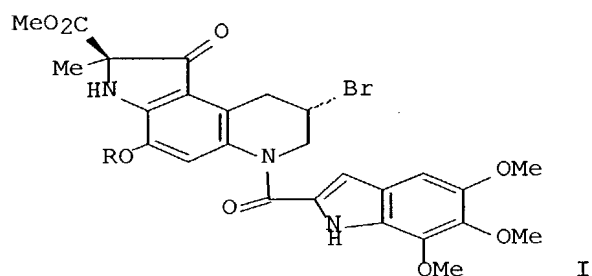
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2995-2998
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

DT Journal

LA English

GI



AB The water-soluble duocarmycin B1 prodrugs such as I (R = β -D-glucopyranosyl; (OH)2OP; N-methylpiperazinylcarbonyl) were synthesized for improving biol. and pharmaceutical profiles of duocarmycin. Among these prodrugs, I (R = N-methylpiperazinylcarbonyl) exhibited potent antitumor activity against several human tumors in vivo.

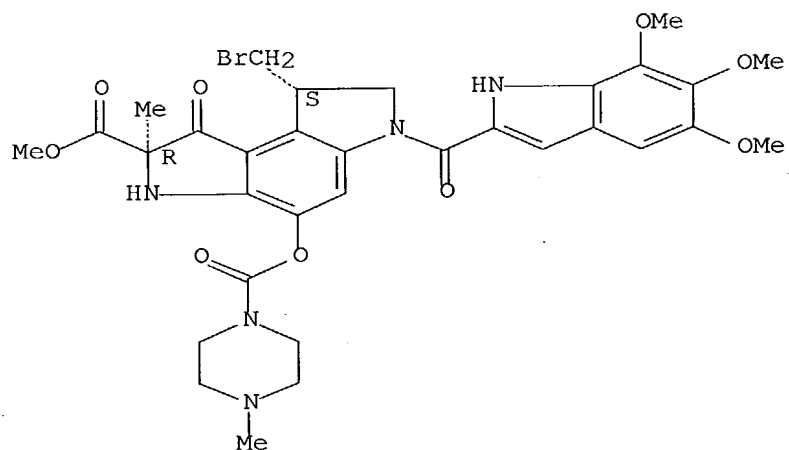
IT 171599-29-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (preparation and antitumor activity of water-soluble duocarmycin B1 prodrugs)

RN 171599-29-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

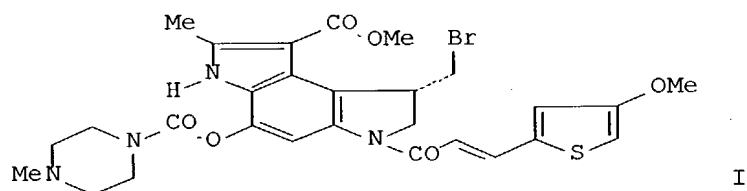
Absolute stereochemistry.



● HCl

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 29 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:674932 CAPLUS Full-text
 DN 132:22791
 TI Synthesis and antitumor activity of duocarmycin derivatives: a-ring
 pyrrole compounds bearing 5-membered heteroarylacryloyl groups
 AU Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji; Okamoto,
 Akihiko;
 Gomi, Katsushige; Saito, Hiromitsu
 CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd.,
 Shizuoka, 411-8731, Japan
 SO Chemical & Pharmaceutical Bulletin (1999), 47(10), 1393-1403
 CODEN: CPBTAL; ISSN: 0009-2363
 PB Pharmaceutical Society of Japan
 DT Journal
 LA English
 OS CASREACT 132:22791
 GI



AB A series of A-ring pyrrole compds. of duocarmycin bearing 5-membered heteroarylacryloyl groups (thienylacryloyl and pyrrolylacryloyl) and heteroarylcarbonyl groups were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. Most of the thienylacrylates displayed in vitro anticellular activity equivalent to 4'-methoxycinnamates. Among the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of methoxy-thienylacrylates, compound I, having 4'-methoxy-2'-thienylacryloyl as segment-B (Seg-B), showed remarkably potent antitumor activity and low peripheral blood toxicity in vivo, which were equal to those of 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates, compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in Seg-B. On the other hand, the 2'-pyrrolylacrylates having a double bond as spacer showed 102- to 103-fold stronger anticellular activity than 2'-pyrrolylcarboxylates (IC50<0.3 nM, 72h-exposure). The 8-O-acetate and 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 2'-pyrrolylacrylates exhibited an antitumor effect at a lower dose compared with the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. with a 4'-methoxycinnamoyl moiety. Moreover, it was expected that the antitumor activity would be increased by the strength of the extra hydrogen bond formed between the nitrogen of the pyrrole amido group and DNA, owing to the increase of the number of N-methyl-2'-pyrrolylcarboxamide units. However, 2'-pyrrolylacrylates having three N-methyl-2'-pyrrolylcarboxamide units showed nearly equal antitumor

activity to 2'-pyrrolylacrylates having only one N-methyl-2'-pyrrolecarboxamide unit.

IT 160819-28-3 186760-06-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)

RN 160819-28-3 CAPLUS

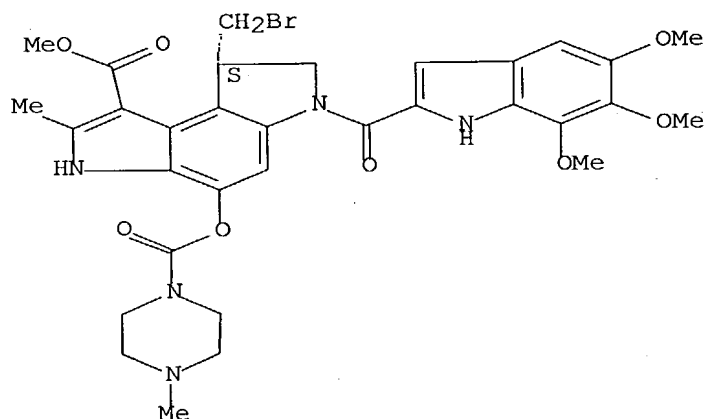
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,

(8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

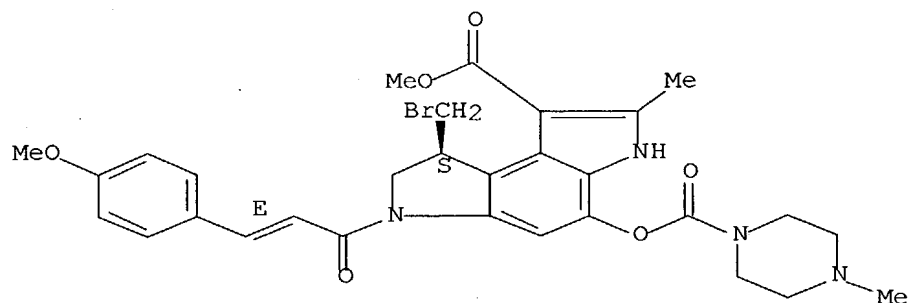
● HBr

RN 186760-06-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



● HCl

IT 251999-64-1P 251999-71-0P 251999-94-7P
251999-95-8P 251999-98-1P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of duocarmycin derivs. bearing
5-membered heteroarylacryloyl groups)

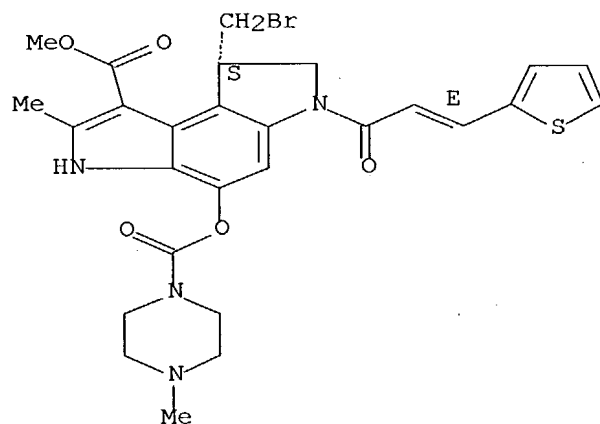
RN 251999-64-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(2E)-1-
oxo-3-(2-thienyl)-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.

Double bond geometry as shown.

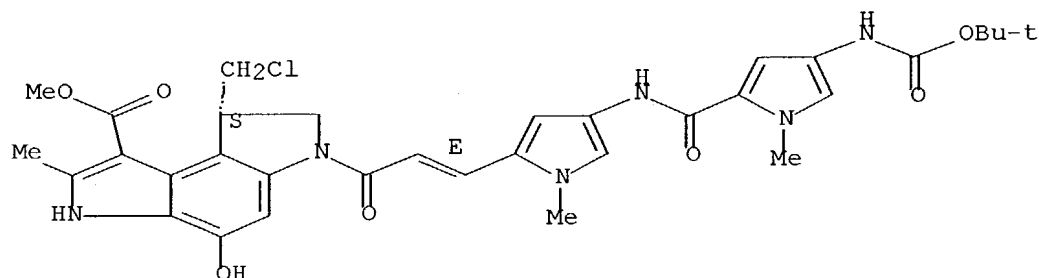


RN 251999-71-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-
[(2E)-3-

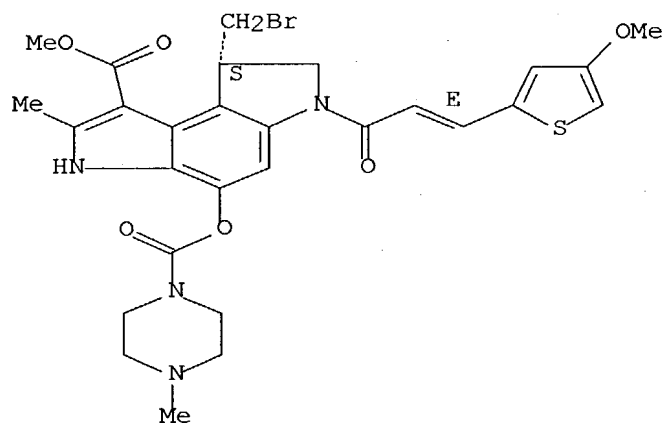
[4-[[[4-[[[(1,1-dimethylethoxy) carbonyl] amino]-1-methyl-1H-pyrrol-2-yl] carbonyl] amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-94-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl) carbonyl] oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

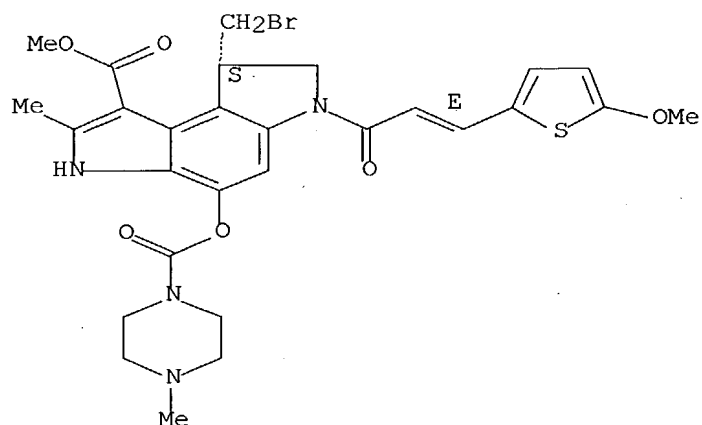
Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-95-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(5-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl) carbonyl] oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 251999-98-1 CAPLUS

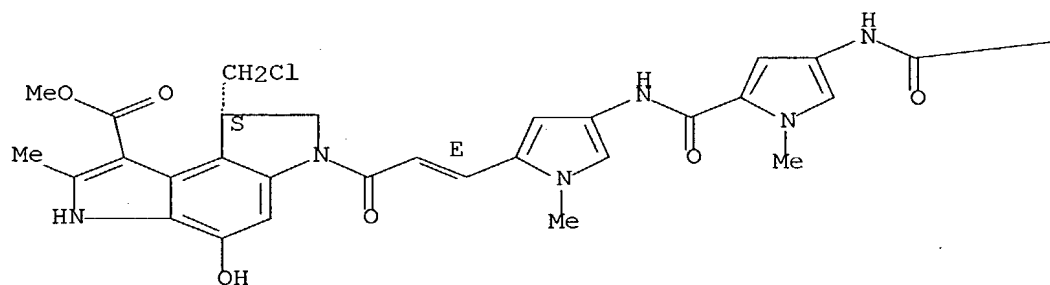
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[(2E)-3-

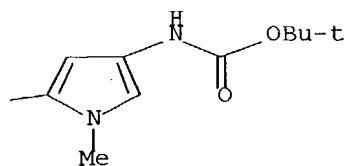
[4-[[[4-[[[4-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A





IT 251999-68-5P 251999-73-2P 251999-74-3P
 251999-75-4P 251999-76-5P 251999-77-6P
 251999-82-3P 251999-83-4P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)

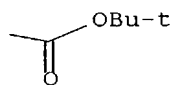
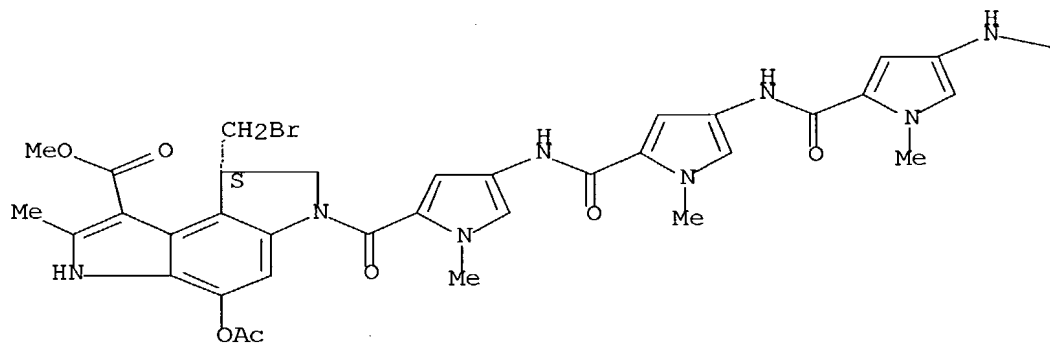
RN 251999-68-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[[4-[[[4-[[[4-[[[1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydro-

2-

methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

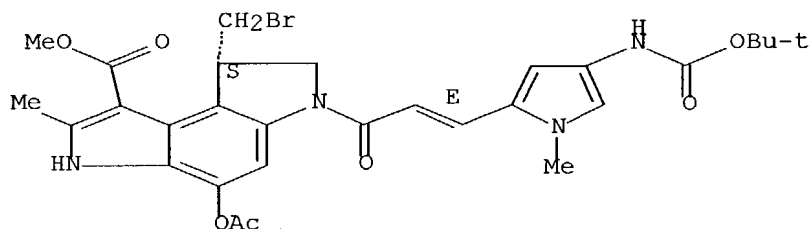
Absolute stereochemistry.



RN 251999-73-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[(2E)-3-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

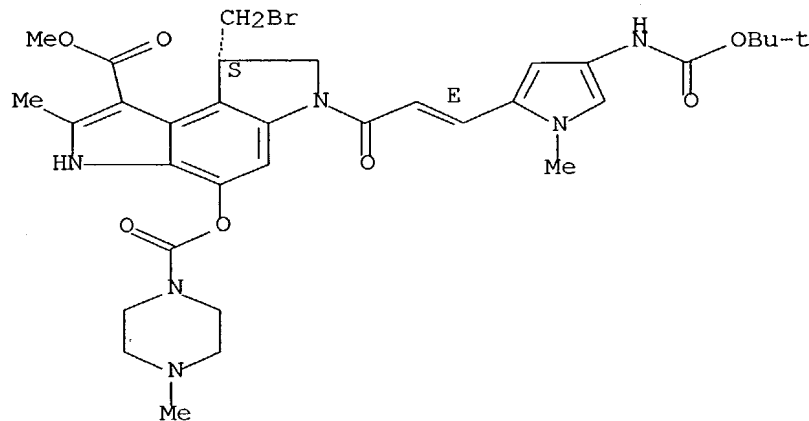
Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-74-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

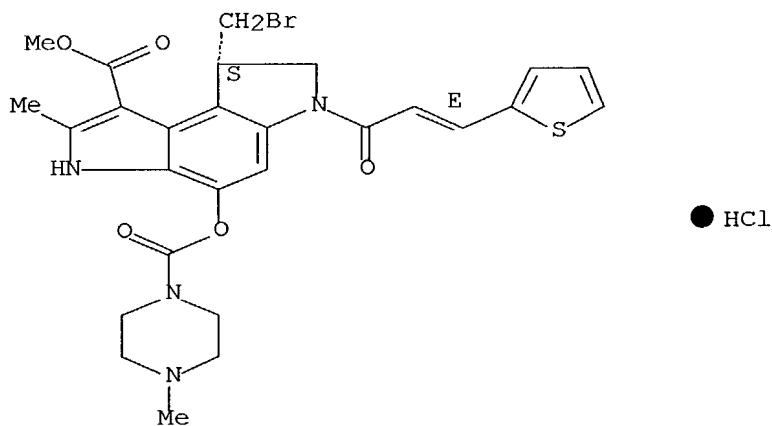
Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-75-4 CAPLUS

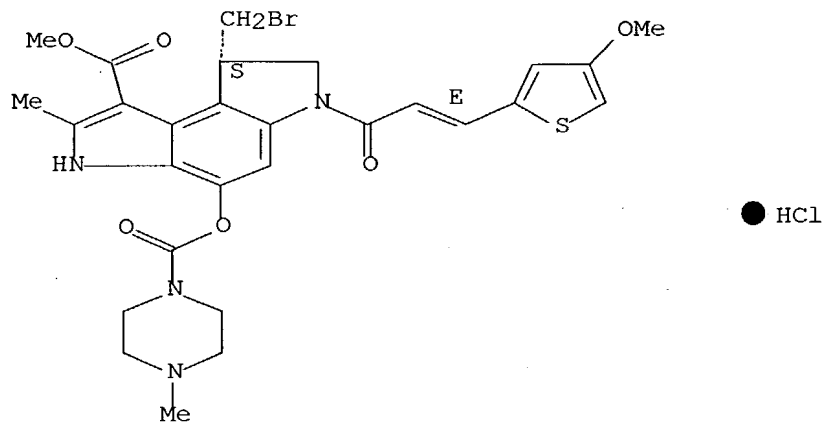
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(2E)-1-oxo-3-(2-thienyl)-2-propenyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-76-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-, methyl ester, monohydrochloride,
(8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

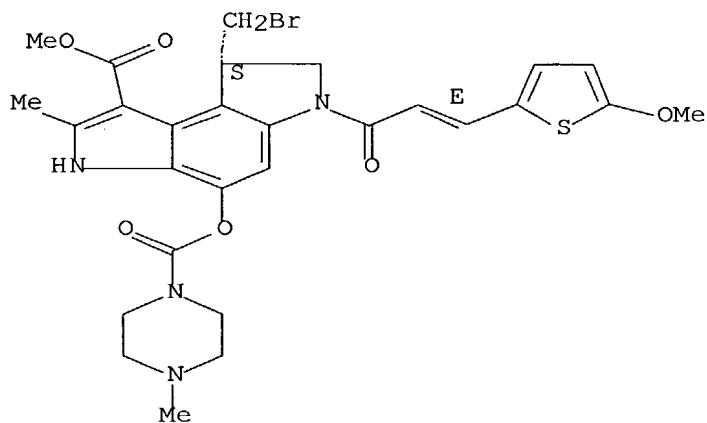


RN 251999-77-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(5-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride,

(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

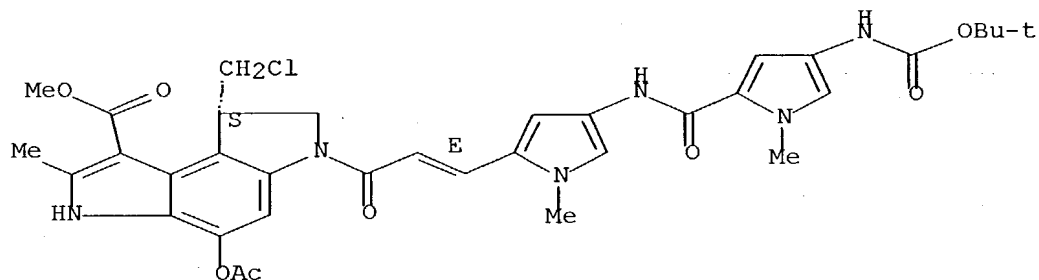


PAGE 2-A

● HCl

RN 251999-82-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[(2E)-3-[4-[[[4-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

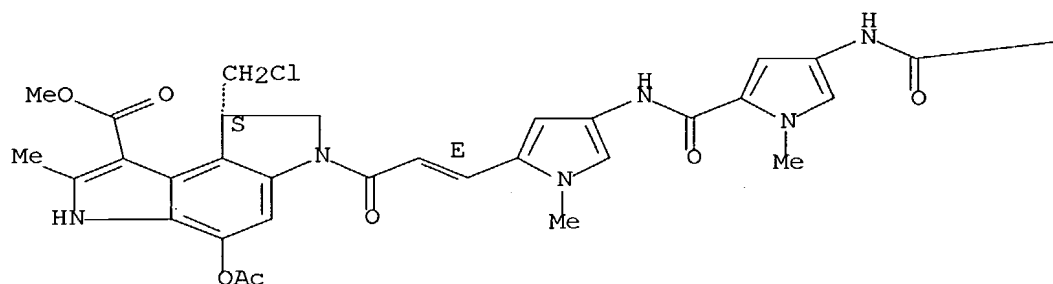


RN 251999-83-4 CAPLUS

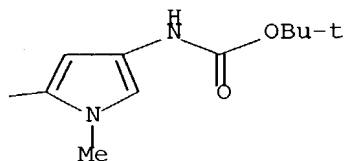
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[(2E)-3-[4-[[[4-[[[4-[[[1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

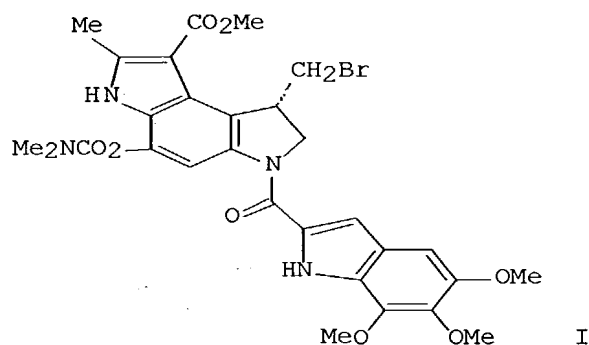


PAGE 1-B



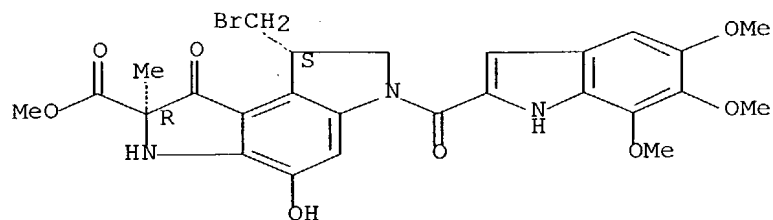
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 30 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:514023 CAPLUS Full-text
 DN 131:322456
 TI Antitumor antibiotics: duocarmycins
 AU Nagamura, Satoru; Saito, Hiromitsu
 CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Tokyo, 194,
 Japan
 SO Chemistry of Heterocyclic Compounds (New York) (Translation of Khimiya
 Geterotsiklicheskikh Soedinenii) (1999), Volume Date 1998, 34(12),
 1386-1405
 CODEN: CHCCAL; ISSN: 0009-3122
 PB Consultants Bureau
 DT Journal
 LA English
 GI



AB Duocarmycin A-ring pyrrole derivs. e.g. I, were prepared from
 duocarmycin B2 and B1 and were evaluated for antitumor activity. The
 IC50 of I against HeLa S3 cells was 55 nM. The antitumor activity and
 relationship between the phys. properties and biol. potency was studied.
 IT **124325-94-6**, Duocarmycin b2 **177958-20-2**
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); RCT (Reactant); BIOL (Biological study); RACT
 (Reactant or reagent)
 (preparation and antitumor activity of duocarmycin derivs.)
 RN 124325-94-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
 indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



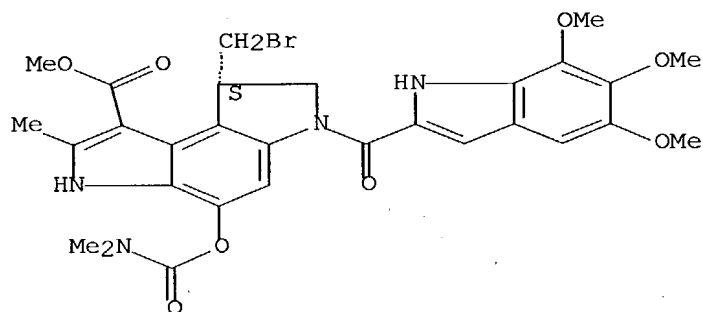
RN 177958-20-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



IT 154889-68-6P 160819-28-3P 177958-19-9P

183240-24-6P 183240-25-7P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)

(preparation and antitumor activity of duocarmycin derivs.)

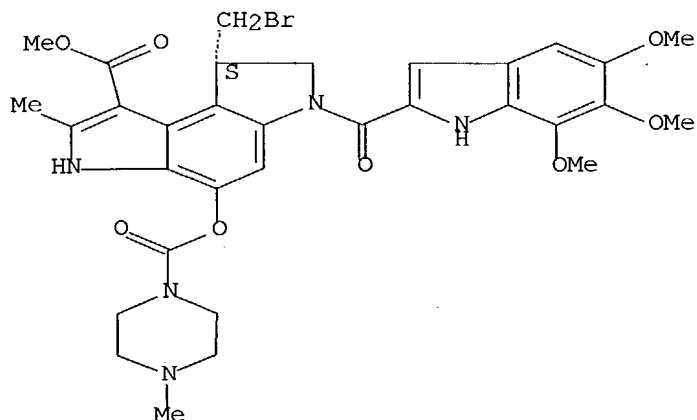
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



RN 160819-28-3 CAPLUS

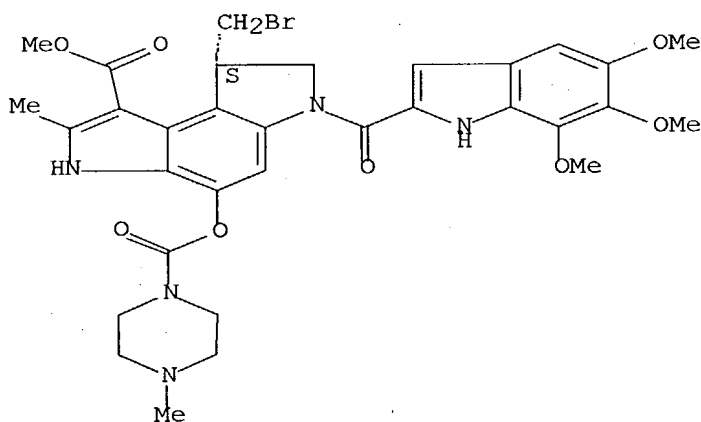
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,

(8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

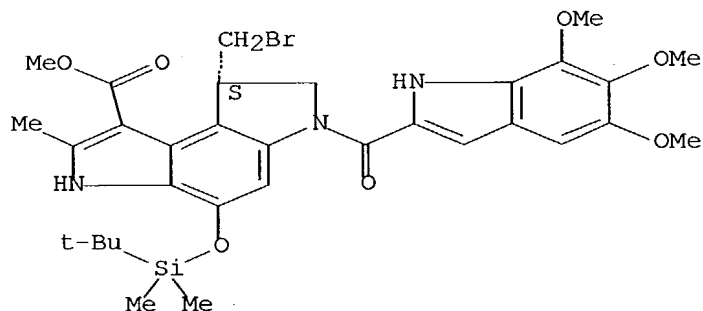
● HBr

RN 177958-19-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

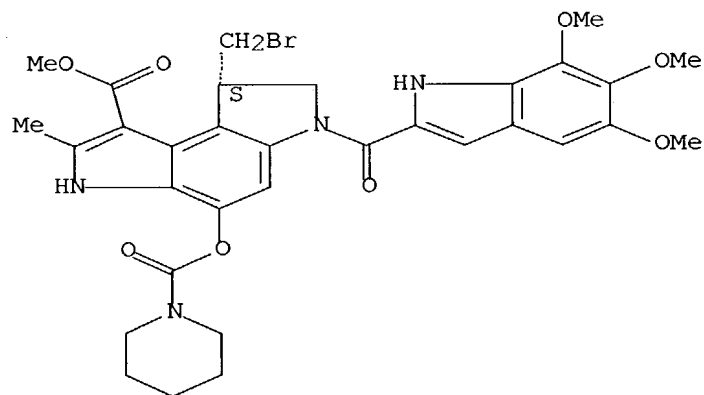
[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



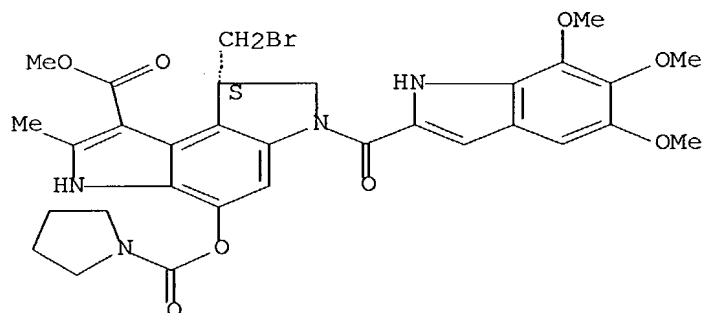
RN 183240-24-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 183240-25-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 129953-15-7P 129953-17-9P 183388-25-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and antitumor activity of duocarmycin derivs.)

RN 129953-15-7 CAPLUS

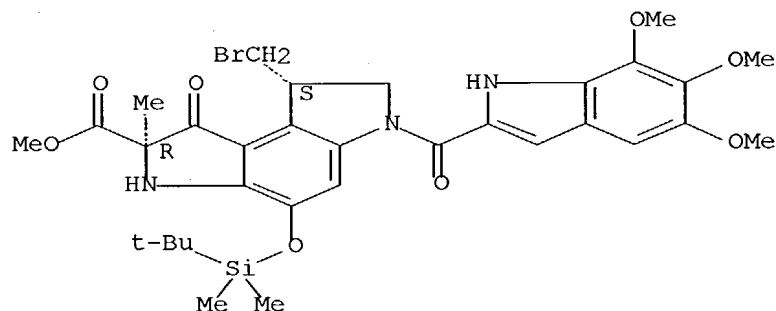
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



RN 129953-17-9 CAPLUS

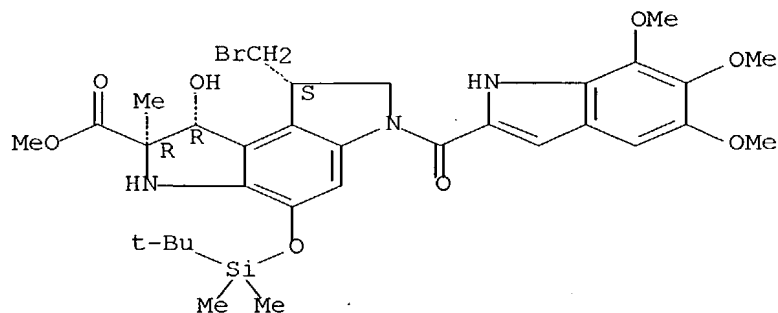
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-
methyl-

6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)-

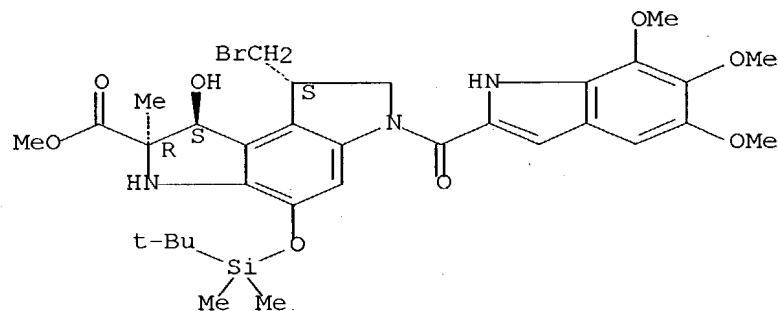
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



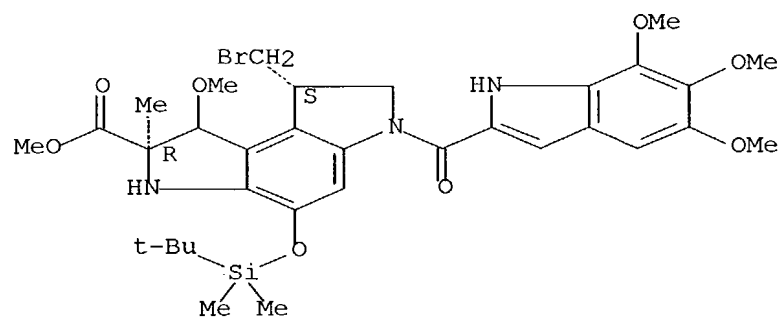
RN 183388-25-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-
 methyl-
 6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2S,8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



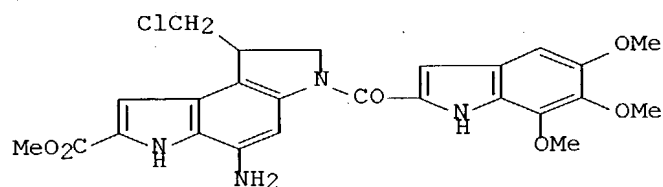
IT 248246-16-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and antitumor activity of duocarmycin derivs.)
 RN 248246-16-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-methoxy-2-
 methyl-
 6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 31 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:439196 CAPLUS Full-text
 DN 131:286298
 TI Synthesis and Cytotoxicity of Amino-seco-DSA: An Amino Analogue of the
 DNA Alkylating Agent Duocarmycin SA
 AU Tercel, Moana; Gieseg, Michael A.; Denny, William A.; Wilson, William R.
 CS Auckland Cancer Society Research Centre Faculty of Medicine and Health
 Science, The University of Auckland, Auckland, 92019, N. Z.
 SO Journal of Organic Chemistry (1999), 64(16), 5946-5953
 CODEN: JOCEAH; ISSN: 0022-3263
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 131:286298
 GI



I

AB This paper describes the synthesis of Me 5-amino-1-(chloromethyl)-3-
 [(5,6,7-trimethoxyindol-2-yl)carbonyl]-1,2-dihydro-3H-pyrrolo[3,2-
 e]indole-7-carboxylate (I), an amino analog of the anticancer
 antibiotic and potent DNA minor groove alkylating agent seco-duocarmycin
 SA. Key points in the synthesis are sequential radical cyclization and
 Hemetsberger reaction steps to construct the indoline and indole rings
 of the target compound from a 1,2,3-trisubstituted benzene precursor.
 An intermediate has been resolved by chiral chromatog. to provide the
 sep. enantiomers of I. Racemic I alkylates DNA at adenine in AT rich
 sequences, similar to seco-duocarmycin SA and the previously reported
 amino-seco-CBI, but is 15-60 times less potent in an in vitro
 cytotoxicity test. Derivs. of I in which the amino group is replaced by
 an electron-withdrawing nitro or nitrobenzylcarbamate substituent are
 considerably less toxic and may have application as prodrugs to be
 activated selectively in a tumor environment.

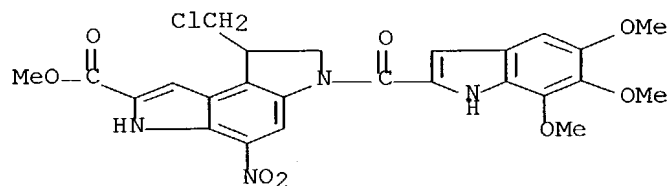
IT 204915-56-0P 204915-57-1P 204915-59-3P
 204915-60-6P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
 (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis and cytotoxicity of amino-seco-DSA, preparation of amino
 analog
 of DNA alkylating agent duocarmycin SA)

RN 204915-56-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-

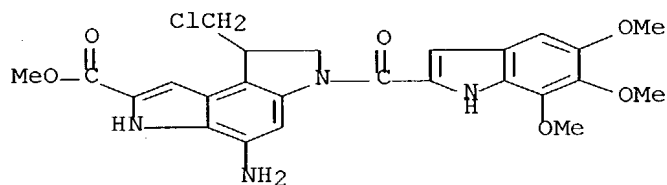
tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 204915-57-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-

,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

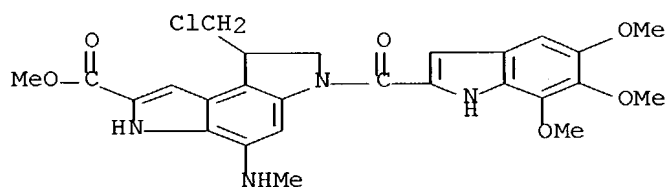


RN 204915-59-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

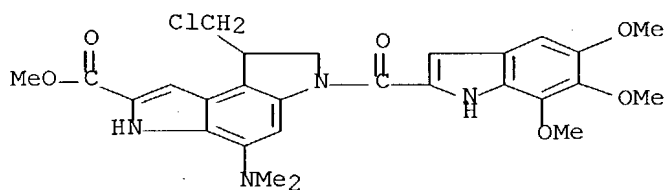
tetrahydro-4-(methylamino)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-

methyl ester (9CI) (CA INDEX NAME)



RN 204915-60-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-(dimethylamino)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



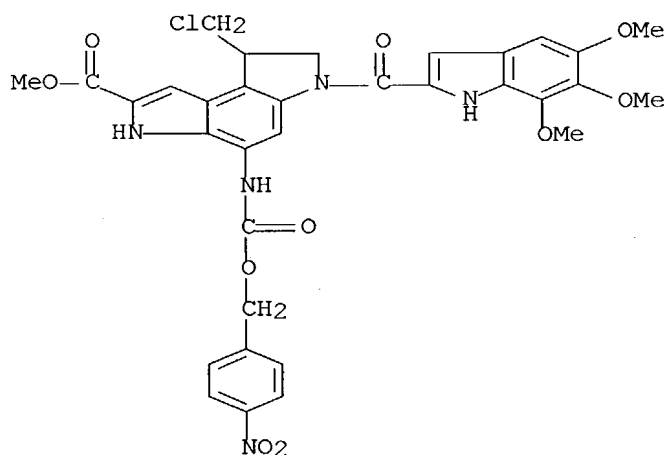
IT 204915-61-7P 246137-60-0P 246137-61-1P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino
analog

of DNA alkylating agent duocarmycin SA)

RN 204915-61-7 CAPLUS

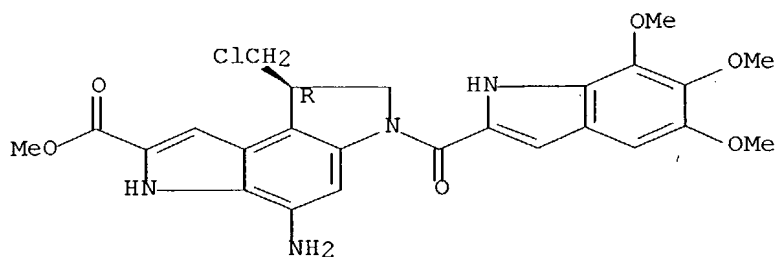
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-[[[(4-nitrophenyl)methoxy]carbonyl]amino]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 246137-60-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-
(chloromethyl)-
,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl
ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

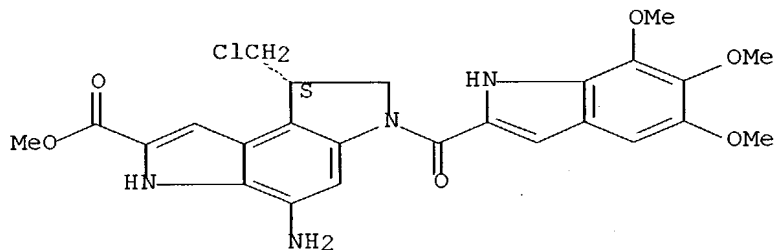


RN 246137-61-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-

,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 246137-54-2P 246137-55-3P

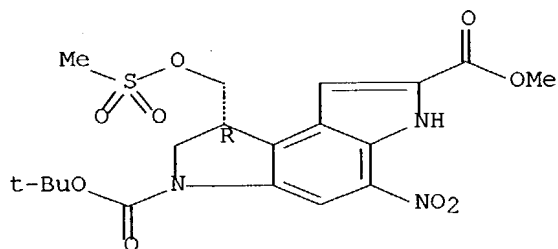
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino analog of DNA alkylating agent duocarmycin SA)

RN 246137-54-2 CAPLUS

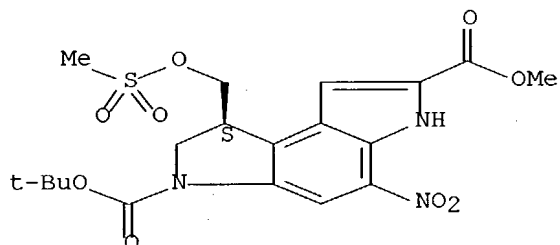
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[[(methylsulfonyl)oxy]methyl]-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 246137-55-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 7,8-dihydro-8-[[(methylsulfonyl)oxy]methyl]-4-nitro-, 6-(1,1-
 dimethylethyl) 2-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 204916-10-9P 204916-11-0P 246137-52-0P
 246137-56-4P 246137-57-5P 246137-58-6P
 246137-59-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

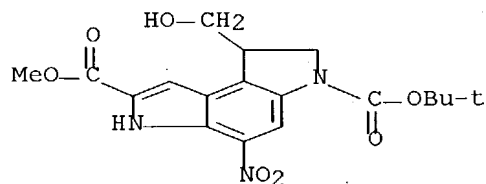
(Reactant or reagent)

(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino
 analog

of DNA alkylating agent duocarmycin SA)

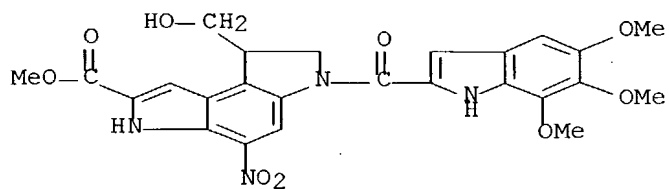
RN 204916-10-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 7,8-dihydro-8-(hydroxymethyl)-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl
 ester (9CI) (CA INDEX NAME)



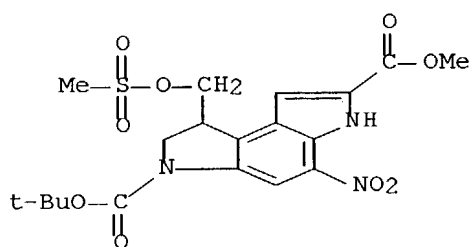
RN 204916-11-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 3,6,7,8-tetrahydro-8-
 (hydroxymethyl)-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl ester (9CI) (CA INDEX NAME)



RN 246137-52-0 CAPLUS

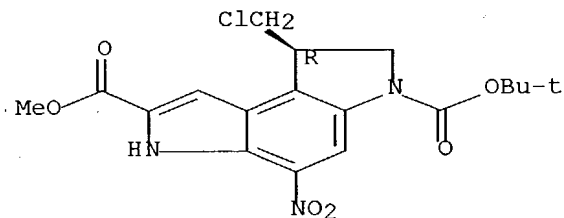
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
7,8-dihydro-8-[[(methylsulfonyl)oxy]methyl]-4-nitro-, 6-(1,1-
dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 246137-56-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8R)- (9CI) (CA INDEX NAME)

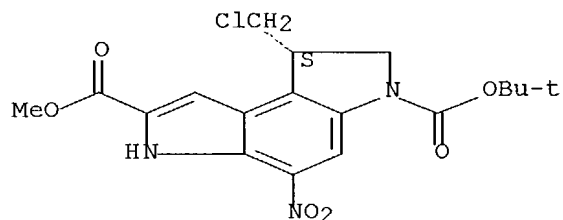
Absolute stereochemistry. Rotation (-).



RN 246137-57-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

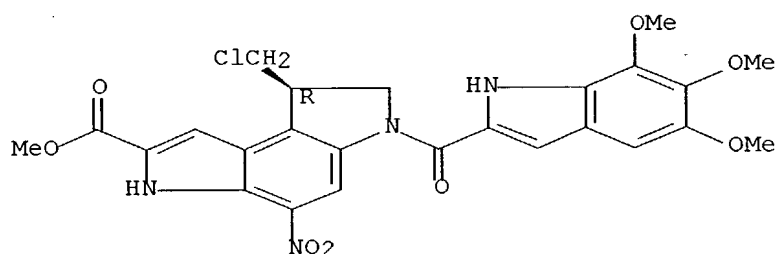


RN 246137-58-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

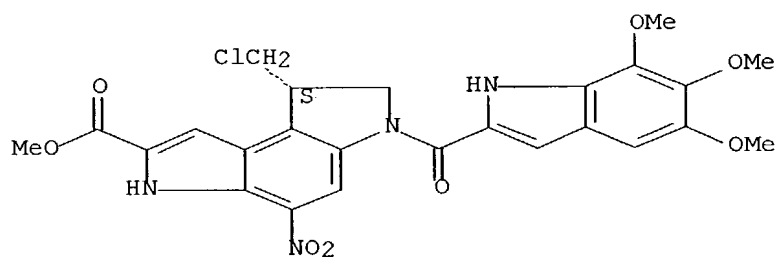


RN 246137-59-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

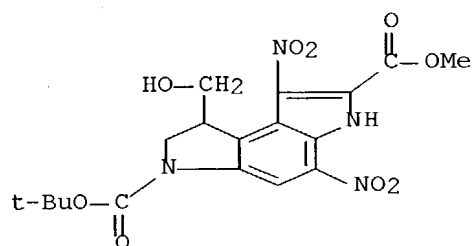


IT 246137-63-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino analog

of DNA alkylating agent duocarmycin SA)
 RN 246137-63-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 7,8-dihydro-8-(hydroxymethyl)-1,4-dinitro-, 6-(1,1-dimethylethyl) 2-
 methyl
 ester (9CI) (CA INDEX NAME)



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 32 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:431081 CAPLUS Full-text

DN 131:286297

TI Synthesis and Antitumor Activity of Duocarmycin Derivatives:

Modification

of Segment-A of A-Ring Pyrrole Compounds

AU Amishiro, Nobuyoshi; Okamoto, Akihiko; Murakata, Chikara; Tamaoki, Tatsuya; Okabe, Masami; Saito, Hiromitsu

CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company Ltd., Nagaizumi Sunto Shizuoka, 411-8731, Japan

SO Journal of Medicinal Chemistry (1999), 42(15), 2946-2960

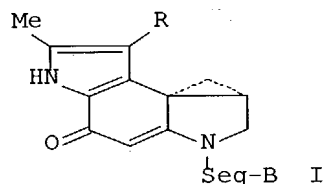
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

GI



AB A series of 3-substituted A-ring pyrrole compds. of duocarmycin were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. These compds. were evaluated for peripheral blood toxicity and delayed lethal toxicity. Further, to expand the investigation of their peripheral blood toxicity, the toxicity to bone marrow cells (CFU-GM, CFU-Meg) was investigated. Among 3-substituted A-ring pyrrole compds. of duocarmycin bearing a 5',6',7'-trimethoxy-2'-indolecarboxyl (Q) group as segment-B, several analogs showed remarkably potent antitumor activity with low peripheral blood toxicity. The 3-formyl compound I [R = CHO, seg-B = Q] showed stronger antitumor activity with lower toxicity to bone marrow cells than DU-86, an active metabolite of KW-2189. However, this compound caused delayed death. On the other hand, the 3-bromo compound I [R = Br, seg-B = 4-methoxycinnamoyl] showed the most potent antitumor activity among the 4'-methoxycinnamate analogs with low toxicity to bone marrow cells. Furthermore, this compound did not cause delayed death. These results would indicate the importance of the C-3 substituents of A-ring pyrrole duocarmycin derivs. for exhibiting antitumor activity and decreasing toxicity.

IT 129953-15-7 177958-19-9 246034-79-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and antitumor activity of duocarmycin derivs. with

modified

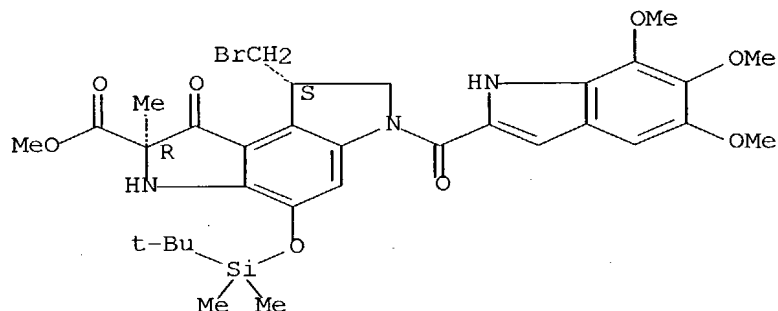
segment-A)

RN 129953-15-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[[1,1-

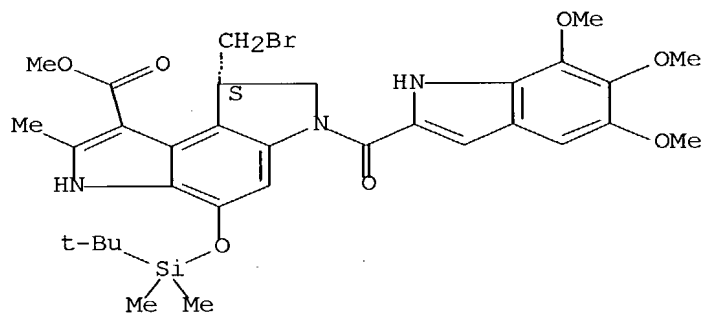
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-
 (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



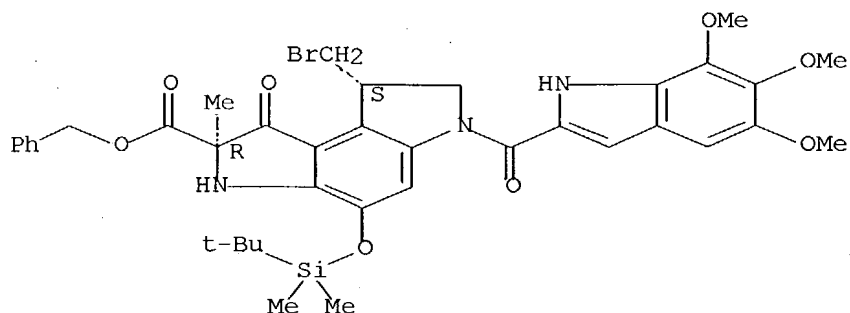
RN 177958-19-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
 INDEX
 NAME)

Absolute stereochemistry.



RN 246034-79-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester,
 (2R,8S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 205050-84-6P 205051-09-8P 205051-11-2P
 205051-57-6P 205051-58-7P 246034-75-3P
 246034-76-4P 246034-77-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and antitumor activity of duocarmycin derivs. with
 modified

segment-A)

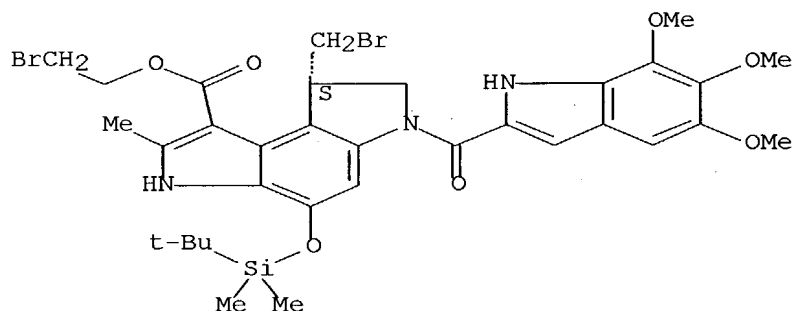
RN 205050-84-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, 2-bromoethyl ester, (8S)- (9CI)

(CA

INDEX NAME)

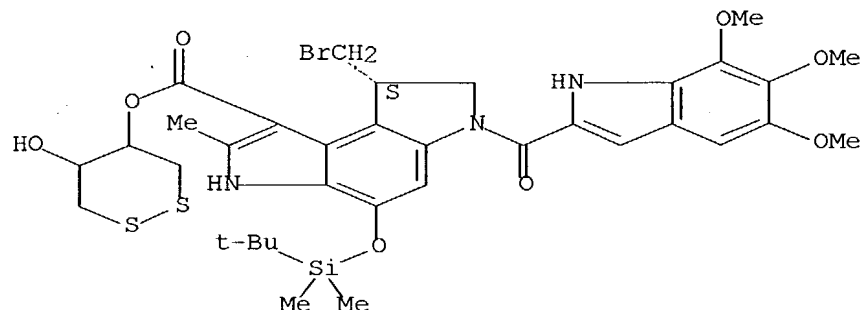
Absolute stereochemistry.



RN 205051-09-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, 5-hydroxy-1,2-dithian-4-yl ester,
 (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



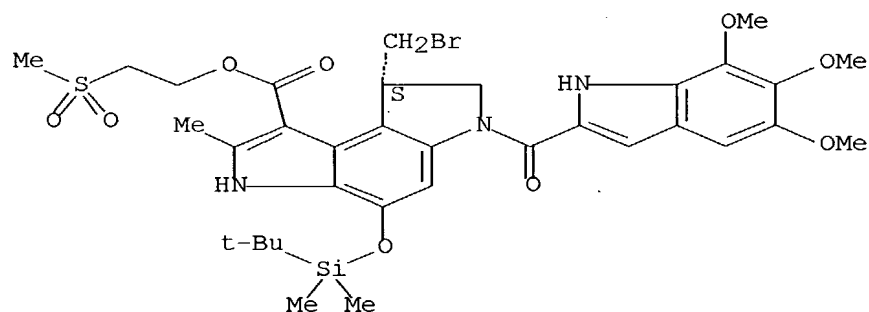
RN 205051-11-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-(methylsulfonyl)ethyl ester, (8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

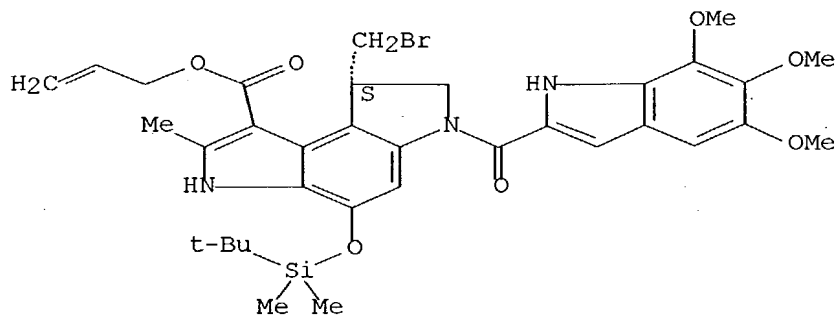


RN 205051-57-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

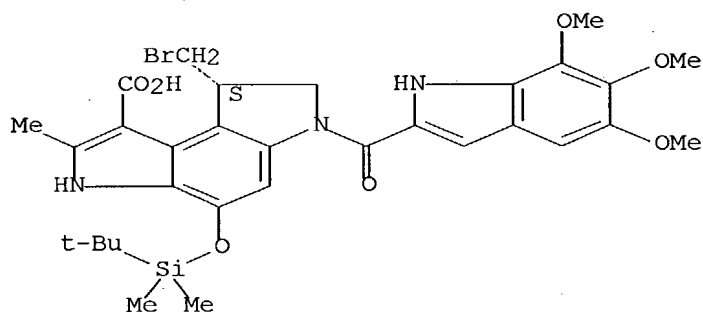


RN 205051-58-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

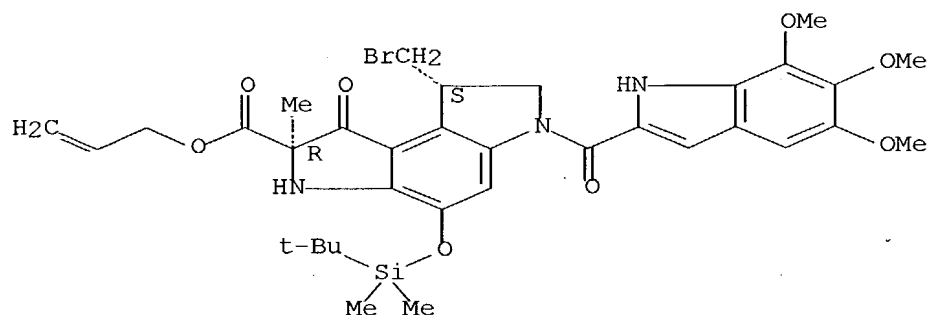


RN 246034-75-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

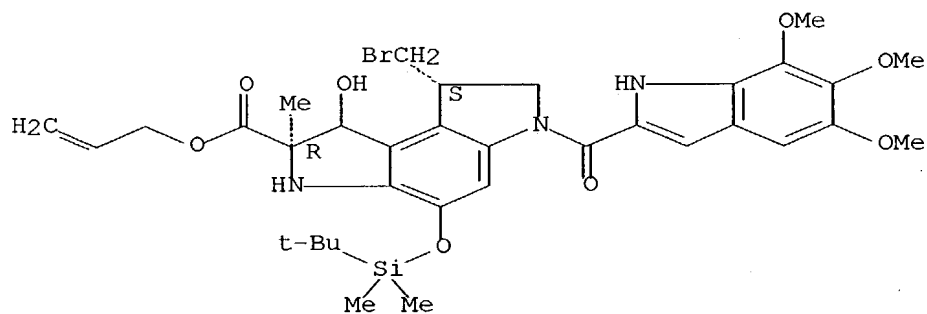
[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



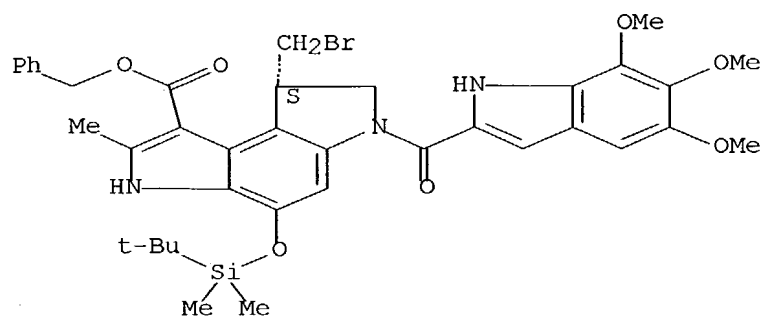
RN 246034-76-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-
 methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester,
 (2R, 8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 246034-77-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester, (8S)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 33 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:352031 CAPLUS Full-text

DN 131:153510

TI Binding-Induced Activation of DNA Alkylation by Duocarmycin SA: Insights from the Structure of an Indole Derivative-DNA Adduct

AU Schnell, Jason R.; Ketchum, Randal R.; Boger, Dale L.; Chazin, Walter J.

CS Departments of Molecular Biology and Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA,

92037,

USA

SO Journal of the American Chemical Society (1999), 121(24), 5645-5652

CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

AB The mechanism for catalysis of DNA alkylation by the potent antitumor antibiotic duocarmycin SA (DSA) has been probed by determining the structure of a DNA adduct of the indole analog (DSA-indole, DSI) lacking three methoxy functional groups. The three-dimensional structure of DSI covalently bound to A19 in d-(G1ACTAATTGAC11)·d-(G12TCAATTAGTC22) was determined by 1H NMR spectroscopy using a total of 935 exptl. distance and dihedral angle constraints. The representative ensemble of 20 conformers has no distance restraint violations greater than 0.03 Å, no torsional restraint violations greater than 0.7°, and a pairwise rmsd over all atoms in the binding site of 0.48 Å. Comparison of the structures of the DSA and DSI adducts reveals a structural basis for the critical role of one of the trimethoxy-indole functional groups in alkylation reactivity. A deeper penetration into the DNA minor groove in the vicinity of the indole subunit is observed for the DSI vs. the DSA adduct, along with some variations in the width and depth of the minor groove throughout the binding site. The most significant difference between the DSI and DSA adducts is the 8° smaller twist of the two ligand subunits in DSI, which correlates with its .apprx.20-fold slower rate of DNA alkylation. This comparison of the structures of the DSI and DSA adducts to the same DNA duplex provides the most direct evidence to date in support of the proposal that the binding of the ligand in the DNA minor groove and consequent twisting of the two ligand subunits, disrupting vinylogous amide stabilization and thereby activating the conjugated cyclopropane electrophile, plays a central role in controlling DNA alkylation reactivity.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 34 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:210305 CAPLUS Full-text
DN 130:338038
TI Novel cyclopropapyrroloindole derivative (AT-3510) bearing
methoxycarbonyl
and trifluoromethyl groups
AU Fukuda, Yasumichi; Furuta, Hirosuke; Kusama, Yoshie; Ebisu, Hiroyuki;
Oomori, Yasuo; Terashima, Shiro
CS Central Research Laboratories, Kyorin Pharmaceutical Company Ltd.,
Mitarai
Nogi Tochigi, 329-0114, Japan
SO Journal of Medicinal Chemistry (1999), 42(8), 1448-1458
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI

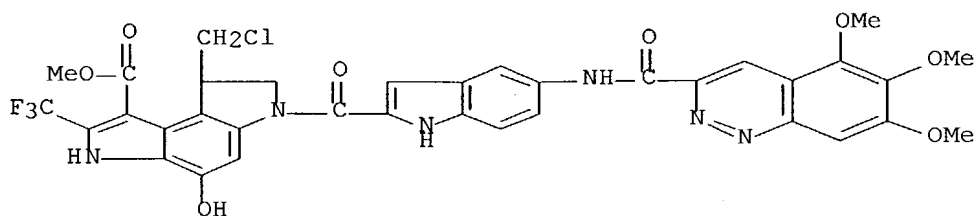
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The seco-Cl 3-methoxycarbonyl-2-trifluoromethylcyclopropapyrroloindole
(MCTFCPI) derivs. dl- and/or (S)-I [Ar = Q, Q1, Q2, Q3, R = 4,5,6-
(MeO)3, 5,6,7-(MeO)3, 5-MeO, etc., X = NH, O, CH, Y = CH, N] carrying
various acyl moieties at the N6-position were synthesized along with
their prodrugs (S)-II, and their antitumor activity was evaluated.
Among these derivs., AT-3510 [(S)-II (Ar = Q1, R = 7-MeO, X = O)], the
novel prodrug MCTFCPI derivative carrying a 5-(7-methoxybenzofuran-2-
ylcarbonyl)aminoindole-2- carbonyl group at the N6-position, was found
to exhibit more excellent antitumor activity against human tumor
xenografts than the clin. trial candidates carzelesin and KW-2189 (III)
and cisplatin.

IT 157823-07-9P 157823-12-6P 157904-26-2P
157904-27-3P 157904-28-4P 157904-29-5P
194093-62-4P 194093-63-5P 194093-64-6P
194093-65-7P 194093-70-4P 224321-44-2P
224321-45-3P 224321-50-0P 224321-51-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT
(Reactant or reagent)
(intermediate in preparation, antitumor activity, and cytotoxicity of
pyrroloindole derivs.)

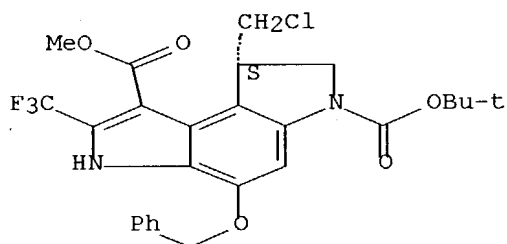
RN 157823-07-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-3-
cinnolinyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI)
(CA INDEX NAME)



RN 157823-12-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

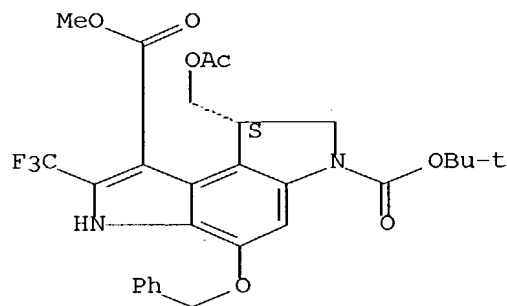
Absolute stereochemistry. Rotation (-).



RN 157904-26-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

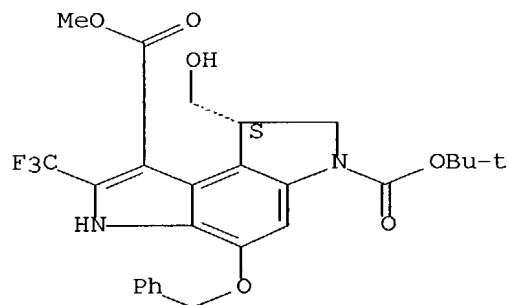


RN 157904-27-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-,

6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

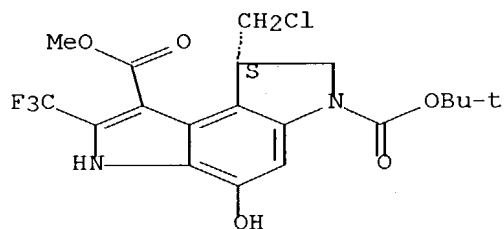
Absolute stereochemistry. Rotation (-).



RN 157904-28-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

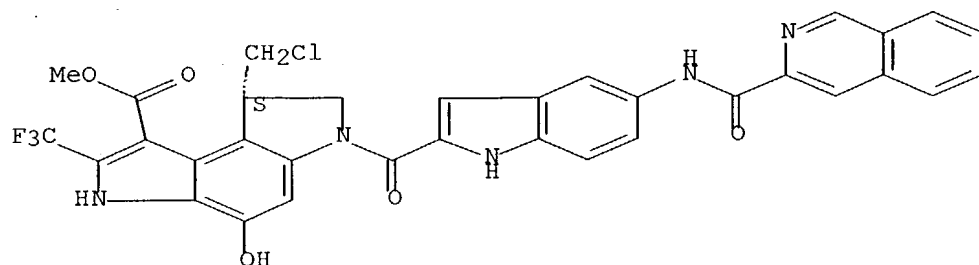
Absolute stereochemistry.



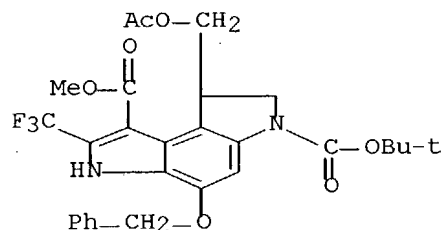
RN 157904-29-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-
yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

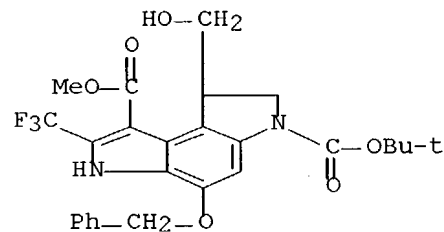
Absolute stereochemistry. Rotation (+).



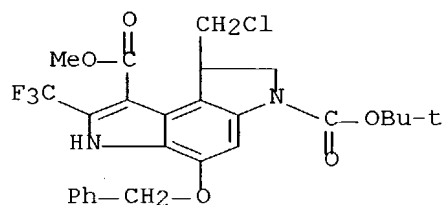
RN 194093-62-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-63-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-,
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

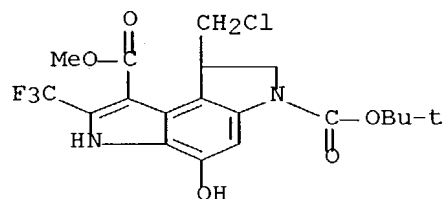


RN 194093-64-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



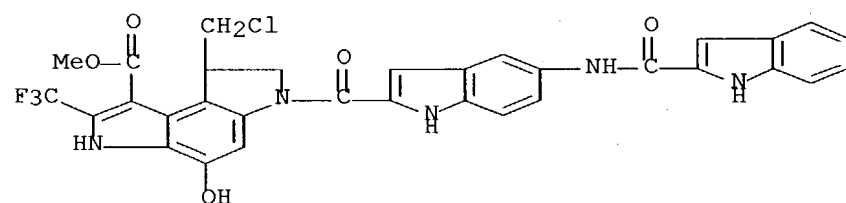
RN 194093-65-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



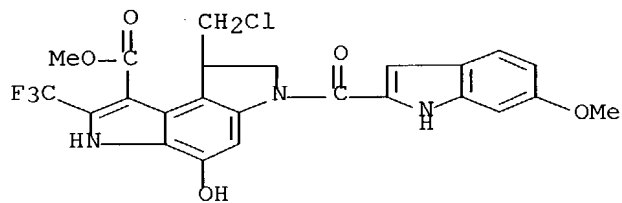
RN 194093-70-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-
yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 224321-44-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(6-methoxy-1H-indol-2-yl)carbonyl]-2-
(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)

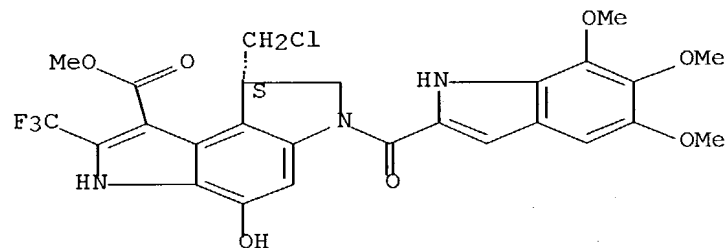


RN 224321-45-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

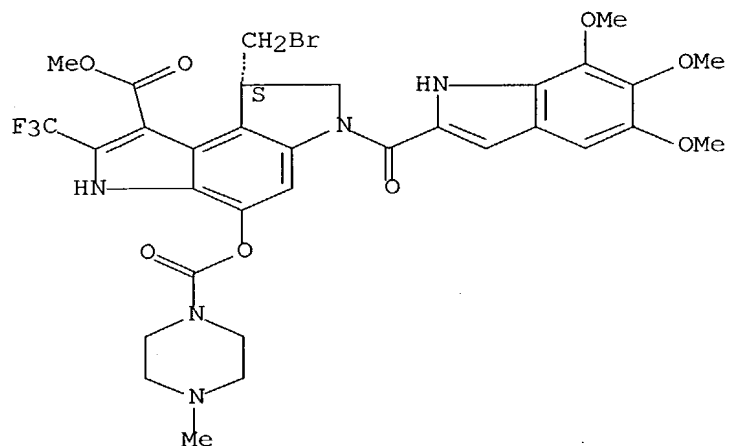


RN 224321-50-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-2-

(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



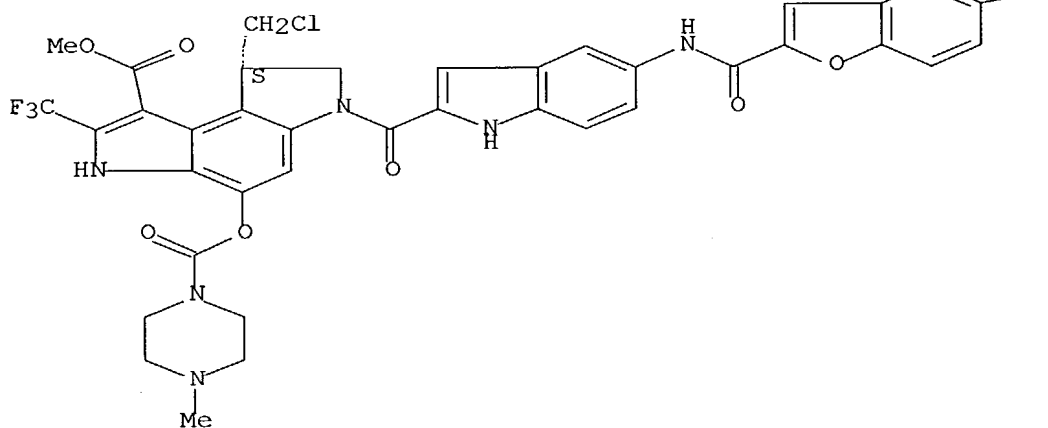
RN 224321-51-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-6-[[5-[[[(5-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-
, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

—OMe

IT 154889-68-6, KW-2189

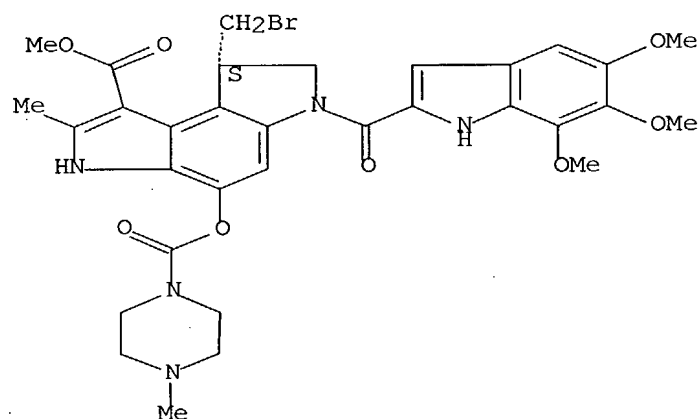
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); BIOL (Biological study)
(preparation, antitumor activity, and cytotoxicity of pyrroloindole
derivs.)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX
NAME)

Absolute stereochemistry.



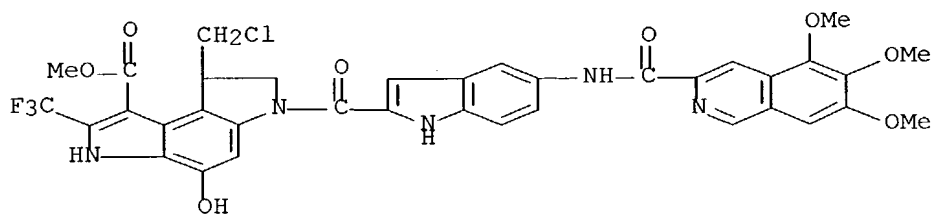
IT 157822-75-8P 157823-25-1P 157823-26-2P
157904-30-8P 157904-32-0P 157904-33-1P
194093-69-1P 194093-71-5P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, antitumor activity, and cytotoxicity of pyrroloindole
derivs.)

RN 157822-75-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[(5,6,7-trimethoxy-3-
isoquinolinyl) carbonyl] amino]-1H-indol-2-yl] carbonyl]-, methyl ester
(9CI)

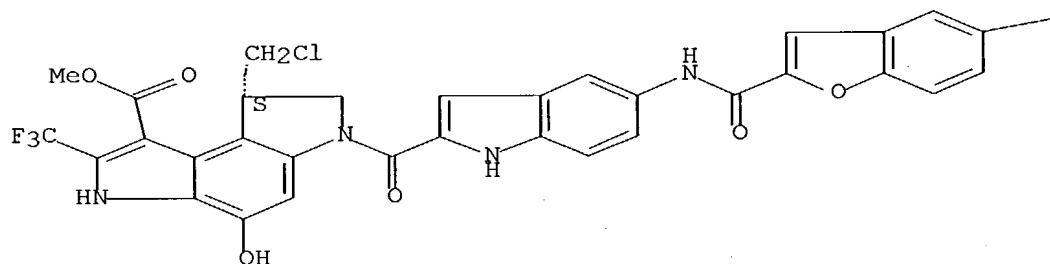
(CA INDEX NAME)



RN 157823-25-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[(5-methoxy-2-benzofuranyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



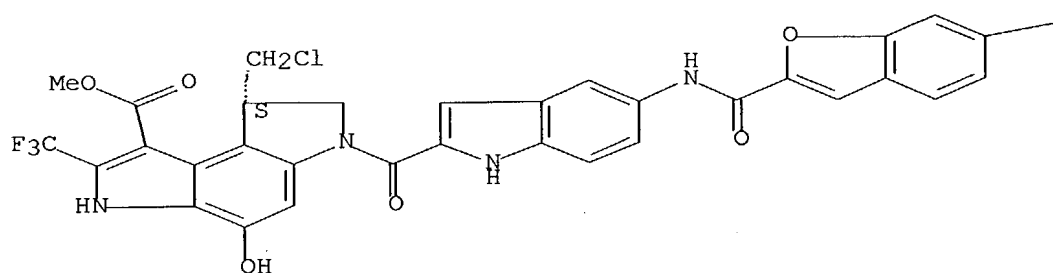
PAGE 1-B

—OMe

RN 157823-26-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[(6-methoxy-2-benzofuranyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



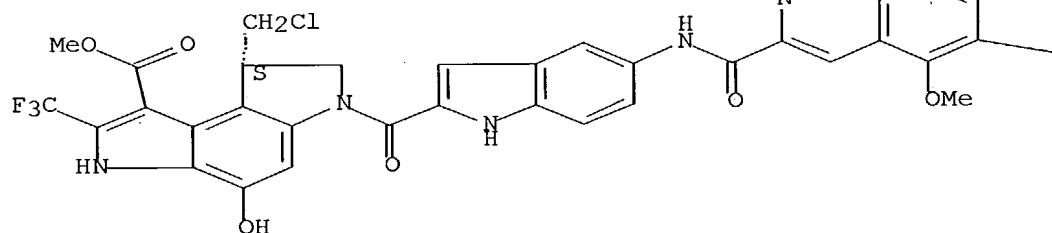
PAGE 1-B

—OMe

RN 157904-30-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[[(5,6,7-trimethoxy-3-
 isoquinolinyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester,
 (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

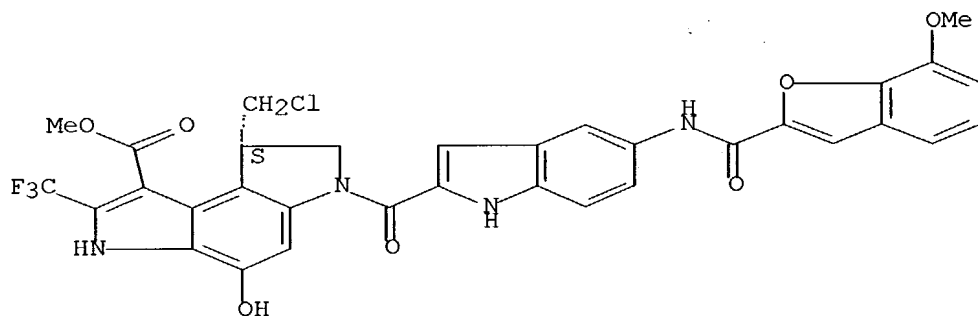
—OMe

—OMe

RN 157904-32-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-
 1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA INDEX NAME)

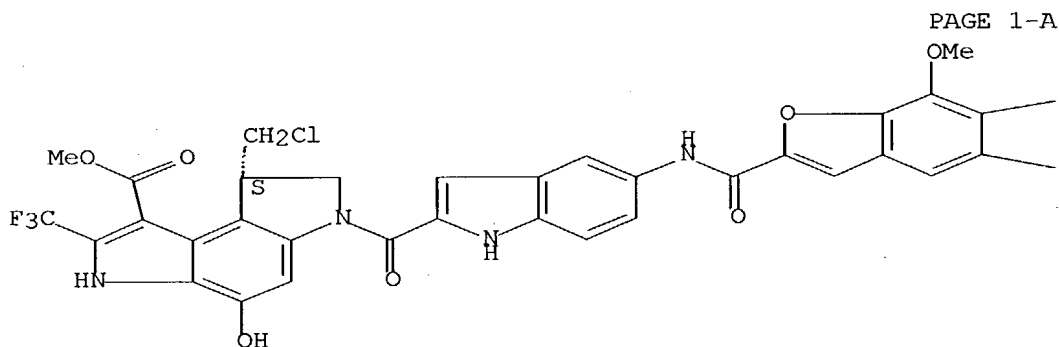
Absolute stereochemistry. Rotation (+).



RN 157904-33-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[[(5,6,7-trimethoxy-2-
 benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester,
 (8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

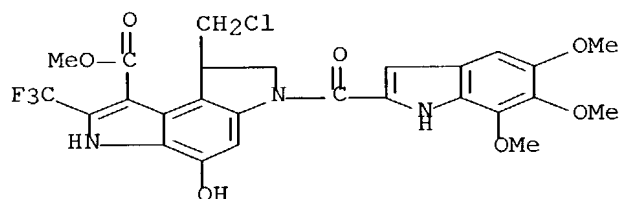


PAGE 1-A

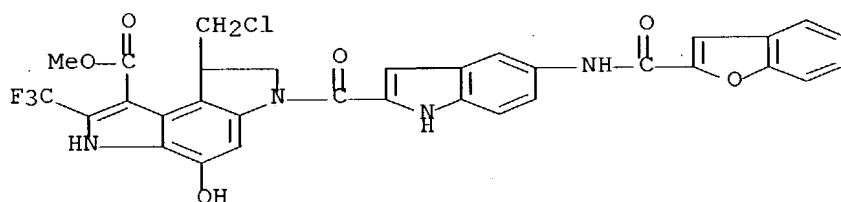
—OMe

—OMe

RN 194093-69-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-
 2-
 yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 194093-71-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-
 benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-
 3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI)
 (CA
 INDEX NAME)

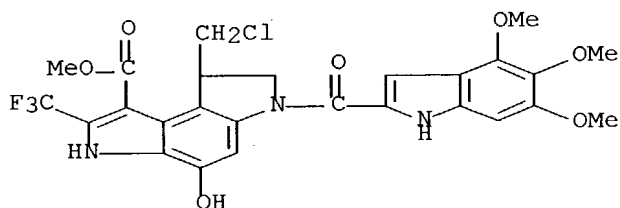


IT 157822-64-5P 157822-69-0P 157822-72-5P
 157822-73-6P 157822-74-7P 157823-18-2P
 157823-24-0P 157823-28-4P 157823-29-5P
 157823-30-8P 157823-31-9P 157823-41-1P
 157823-42-2P 157823-43-3P 157823-45-5P
 157904-34-2P 194361-61-0P 224321-46-4P
 224321-47-5P 224321-52-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation, antitumor activity, and cytotoxicity of pyrroloindole derivs.)

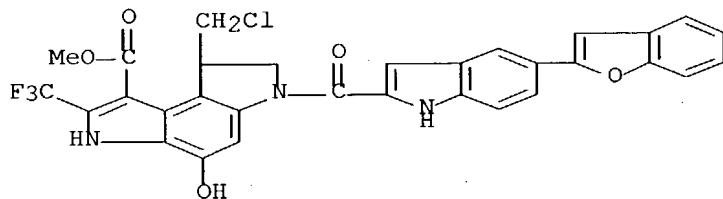
RN 157822-64-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(4,5,6-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



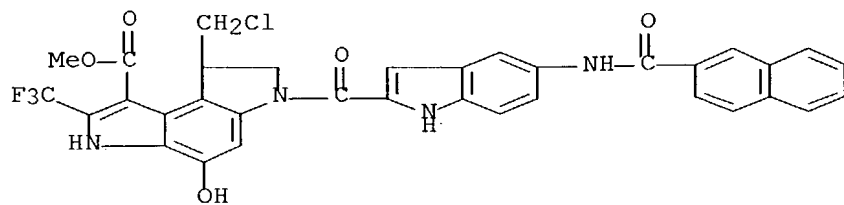
RN 157822-69-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-(2-benzofuranyl)-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)

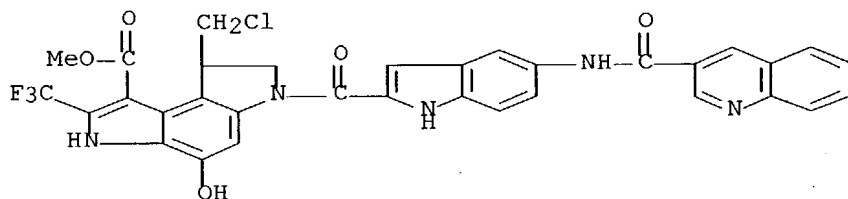


RN 157822-72-5 CAPLUS

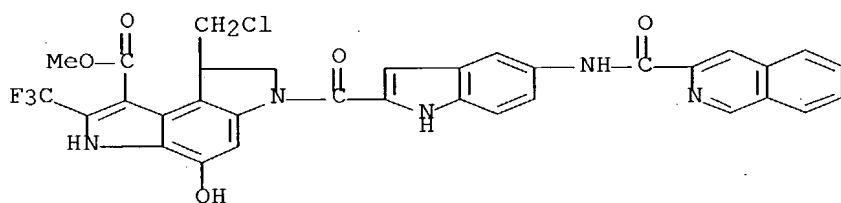
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(2-naphthalenylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157822-73-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[(3-quinolinylcarbonyl)amino]-1H-indol-2-
 yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)

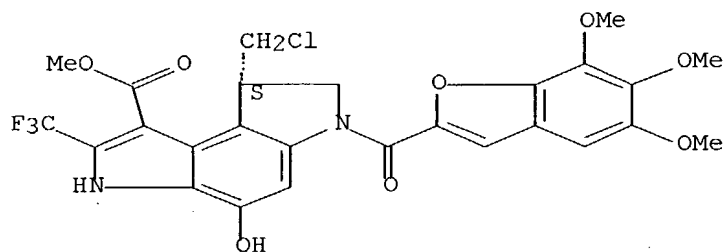


RN 157822-74-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-
 yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157823-18-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-2-
 benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 157823-24-0 CAPLUS

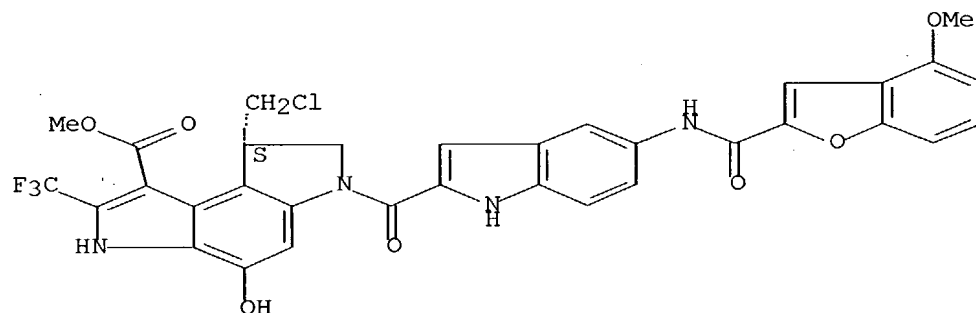
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

1H- tetrahydro-4-hydroxy-6-[[5-[[[(4-methoxy-2-benzofuranyl)carbonyl]amino]-

(CA indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)

INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 157823-28-4 CAPLUS

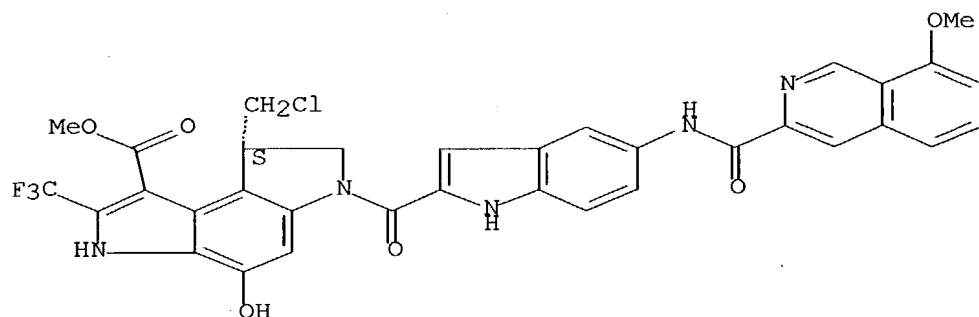
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

1H- tetrahydro-4-hydroxy-6-[[5-[[[(8-methoxy-3-isoquinolinyl)carbonyl]amino]-

(CA indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)

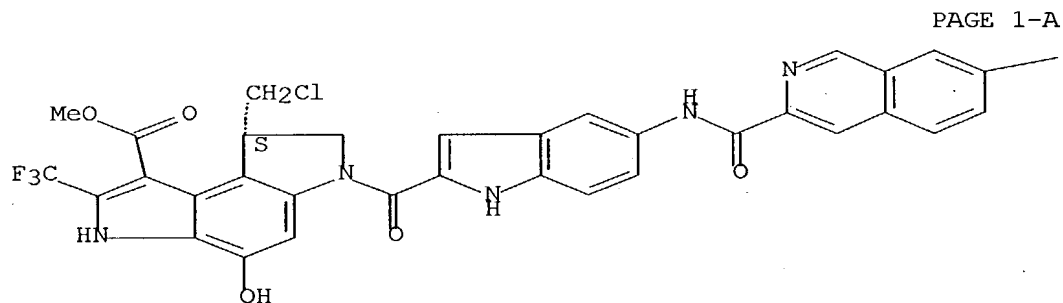
INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 157823-29-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[(7-methoxy-3-isoquinolinyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).



PAGE 1-A

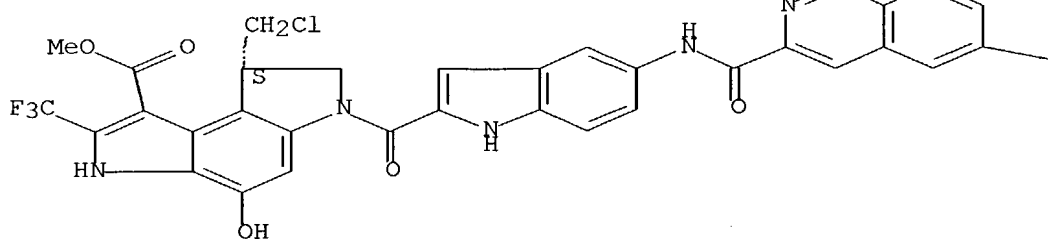
—OMe

PAGE 1-B

RN 157823-30-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[(6-methoxy-3-isoquinolinyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A

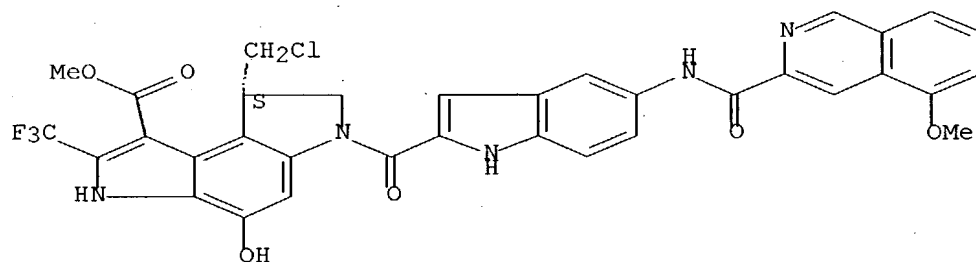


PAGE 1-B

—OMe

RN 157823-31-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[5-methoxy-3-isoquinolinyloxy]carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

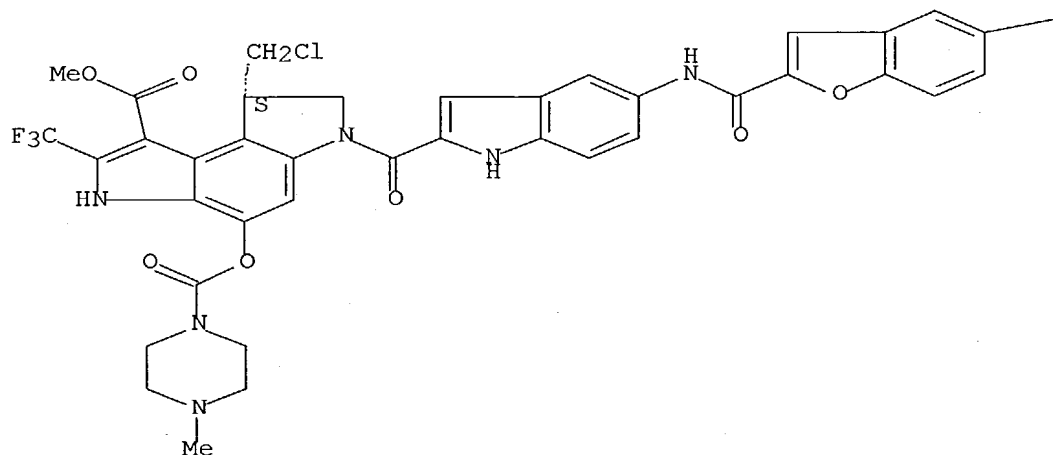


RN 157823-41-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-6-[[5-[[5-methoxy-2-benzofuranyloxy]carbonyl]amino]-1H-indol-2-
 yl]carbonyl]-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-

(trifluoromethyl)-
 , methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



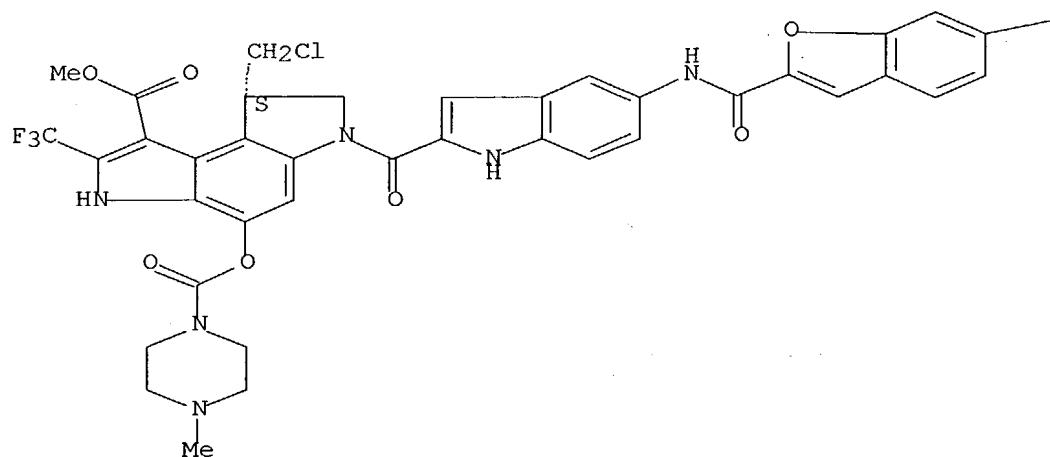
PAGE 1-B

—OMe

● HCl

RN 157823-42-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-6-[[5-[[(6-methoxy-2-benzofuranyl) carbonyl] amino]-1H-indol-2-
 yl] carbonyl]-4-[[(4-methyl-1-piperazinyl) carbonyl] oxy]-2-
 (trifluoromethyl)-
 , methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



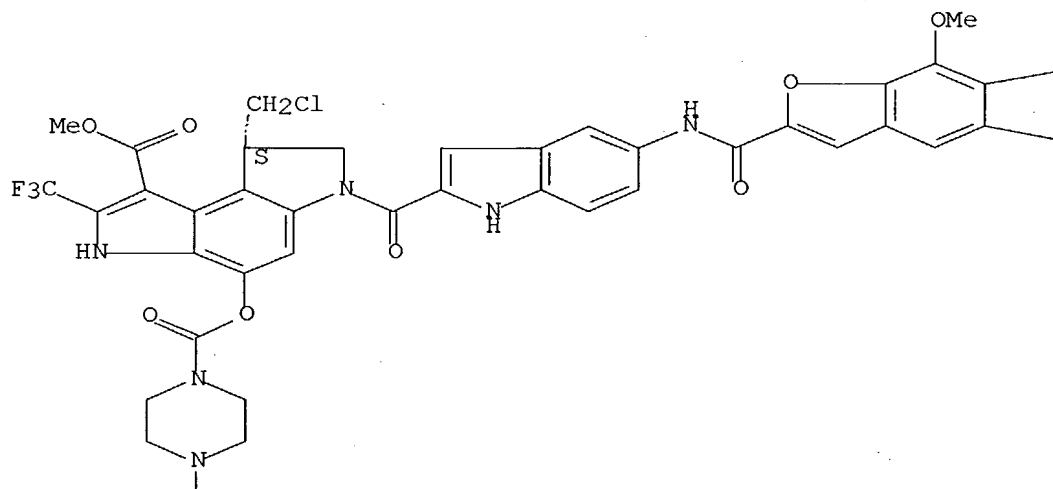
—OMe

● HCl

RN 157823-43-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-6-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-2-
 (trifluoromethyl)-
 6-[[5-[[(5,6,7-trimethoxy-2-benzofuranyl) carbonyl]amino]-1H-indol-2-
 yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

— OMe

— OMe

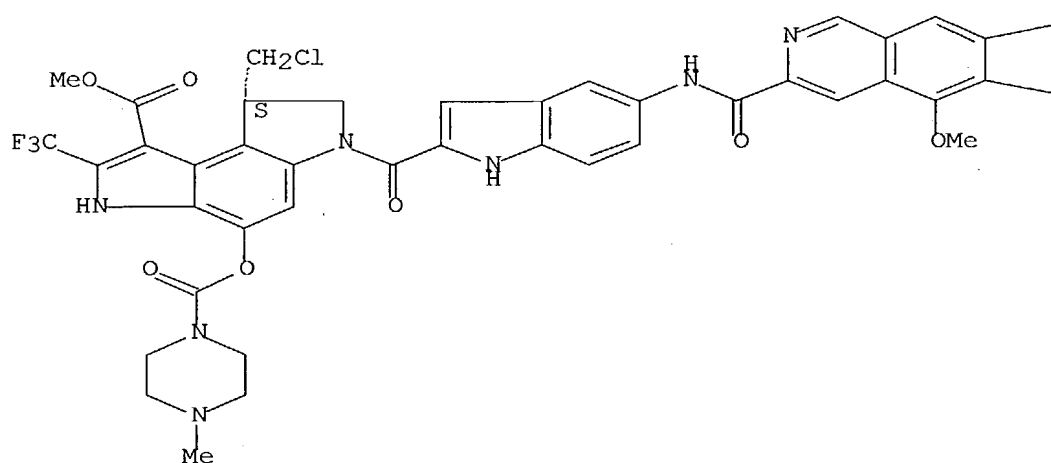
PAGE 2-A

Me

● HCl

RN 157823-45-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-
 (trifluoromethyl)-6-
 [[5-[[5,6,7-trimethoxy-3-isoquinolinyl]carbonyl]amino]-1H-indol-2-
 yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry. Rotation (+).



—OMe

—OMe

● HCl

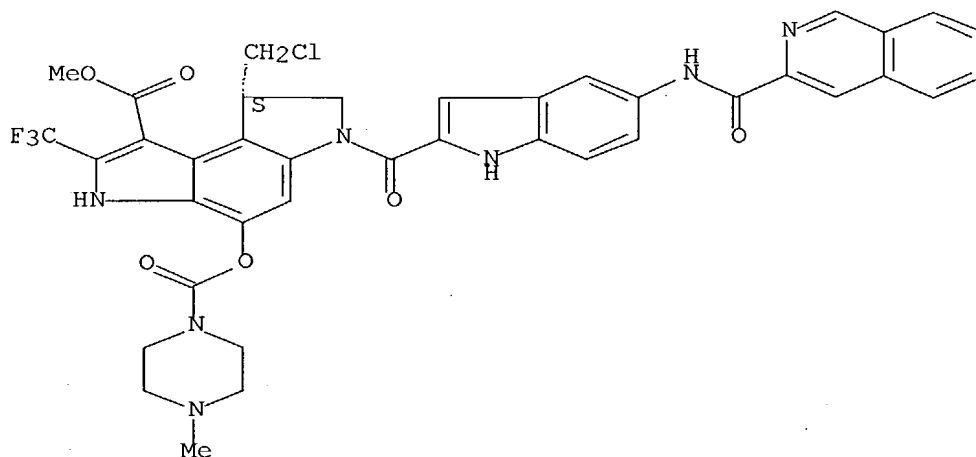
RN 157904-34-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-

4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

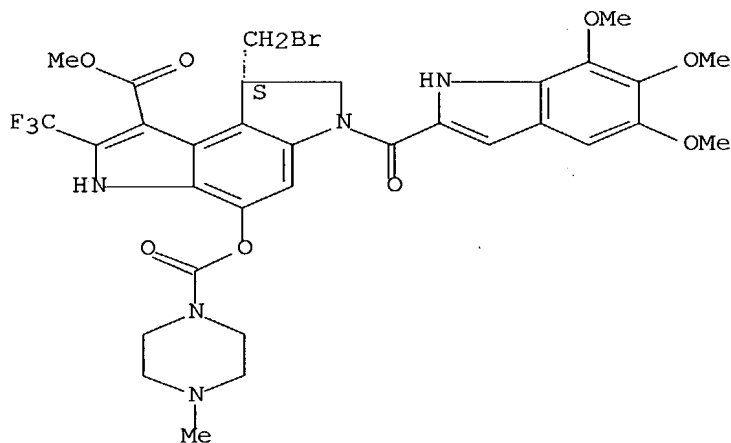


● HCl

RN 194361-61-0 CAPLUS

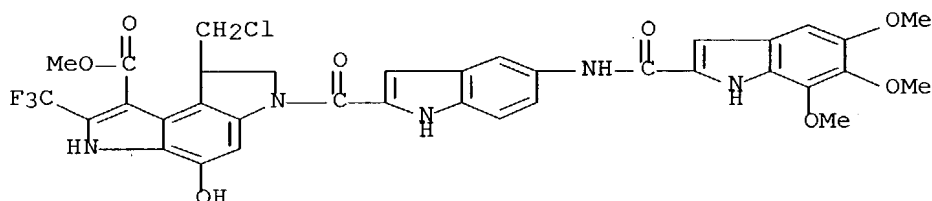
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

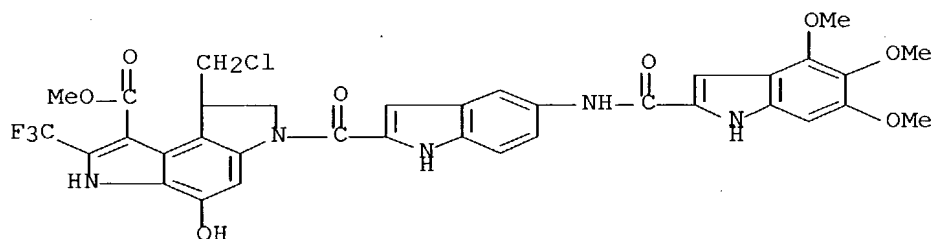


● HCl

RN 224321-46-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI)
(CA INDEX NAME)

RN 224321-47-5 CAPLUS

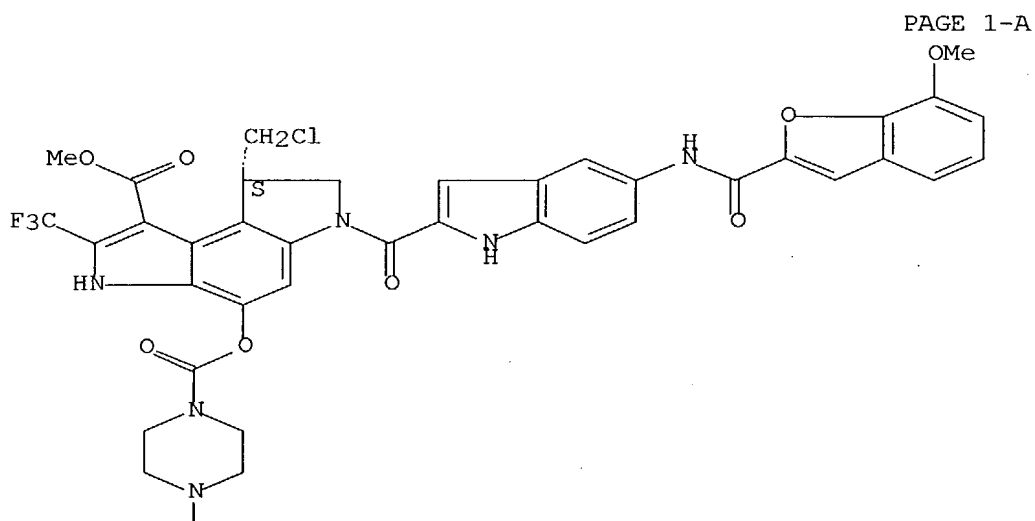
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[4,5,6-trimethoxy-1H-
indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI)
(CA INDEX NAME)

RN 224321-52-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-6-[[5-[[7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-
yl]carbonyl]-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-2-
(trifluoromethyl)-

, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



Me

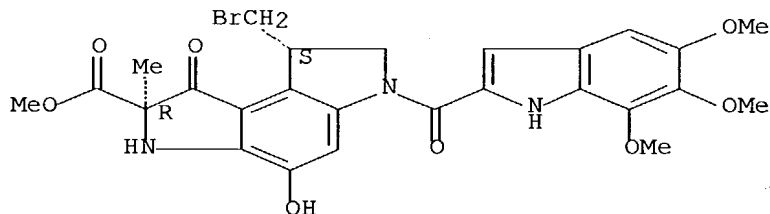
PAGE 2-A

● HCl

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

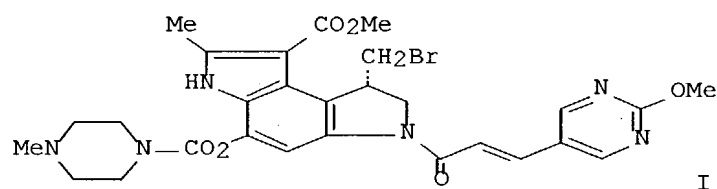
L10 ANSWER 35 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:192822 CAPLUS Full-text
 DN 131:1795
 TI Sequence-specific DNA alkylation by hybrid molecules between segment A
 of
 Duocarmycin A and pyrrole/imidazole diamide
 AU Tao, Zhi-Fu; Fujiwara, Tsuyoshi; Saito, Isao; Sugiyama, Hiroshi
 CS Institute for Medical and Dental Engineering, Tokyo Medical and Dental
 University, Tokyo, 101-0062, Japan
 SO Angewandte Chemie, International Edition (1999), 38(5), 650-653
 CODEN: ACIEF5; ISSN: 1433-7851
 PB Wiley-VCH Verlag GmbH
 DT Journal
 LA English
 AB The authors decide the preparation of novel hybrid mols. between segment
 A of duocarmycin A and pyrrole/imidazole diamides. These hybrids
 primarily alkylate the 3' end of A in AT-rich sequences, as does the
 parent compound, duocarmycin. These hybrids also alkylate G residues of
 predetd. DNA sequences efficiently and with high specificity by
 formation of a heterodimer with distamycin A.
 IT **124325-94-6**, Duocarmycin B2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of duocarmycin A and pyrrole/imidazole diamide hybrid)
 RN 124325-94-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
 indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 36 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:73220 CAPLUS Full-text
 DN 130:252170
 TI New Water-Soluble Duocarmycin Derivatives: Synthesis and Antitumor Activity of A-Ring Pyrrole Compounds Bearing β -Heteroarylacryloyl Groups
 AU Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige;
 Saito, Hiromitsu
 CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company Ltd., Nagaizumi Sunto Shizuoka, 411-0943, Japan
 SO Journal of Medicinal Chemistry (1999), 42(4), 669-676
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 GI



AB A series of A-ring pyrrole compds. of duocarmycin bearing 4'-methoxy- β -heteroarylacryloyl groups were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. Most of the 4'-methoxy- β -heteroarylacrylates displayed in vitro anticellular activity equivalent to that of 4'-methoxycinnamates. Among the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxy- β -heteroarylacrylates, compound I·HCl having a (4-methoxy-3,5-pyrimidinyl)acryloyl as segment-B (Seg-B) showed remarkably potent in vivo antitumor activity and low peripheral blood toxicity compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in Seg-B, which were equal to 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates. Moreover, these 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxy- β -heteroarylacrylates had high aqueous solubility

IT 186760-19-0

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (synthesis and antitumor activity of β -heteroarylacryloyl group bearing pyrrole analogs of duocarmycin)

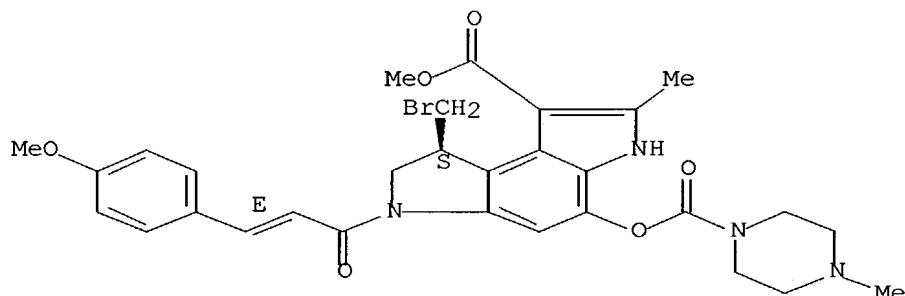
RN 186760-19-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-

[[(4-

methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 118292-36-7DP, Duocarmycin C2, analog 124325-94-6DP,
Duocarmycin B2, analog 221549-89-9P 221549-92-4P
221549-95-7P 221549-99-1P

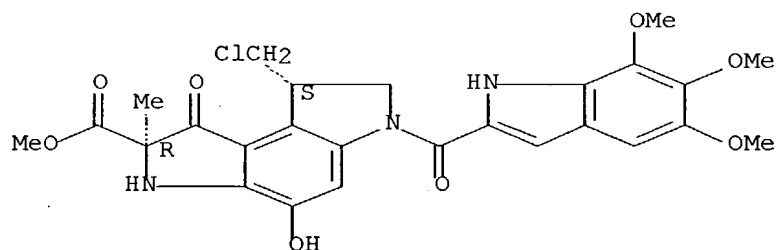
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of β -heteroarylacryloyl group bearing pyrrole analogs of duocarmycin)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

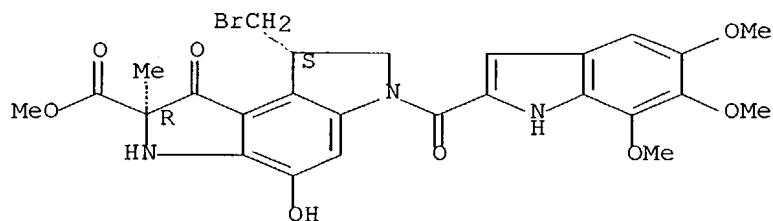
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

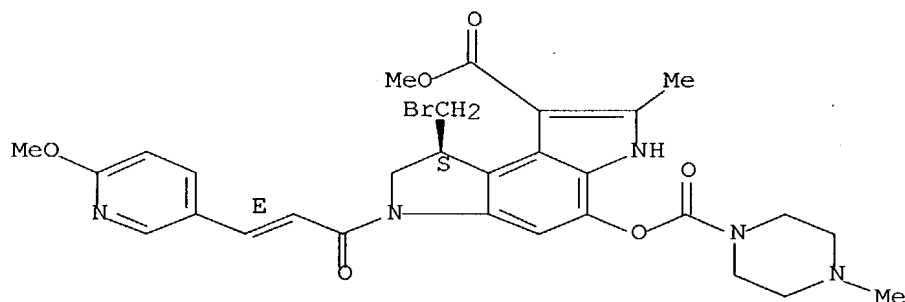
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221549-89-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

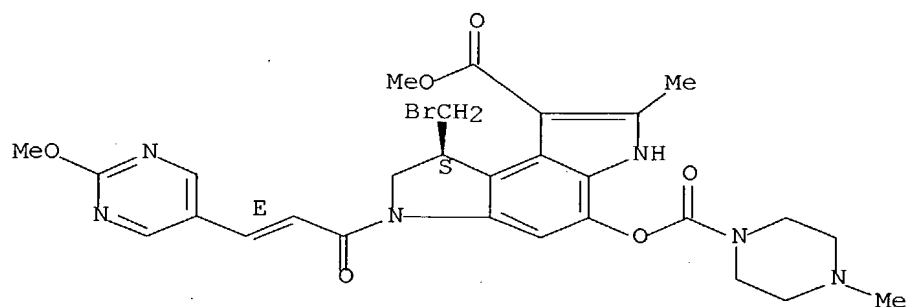
Absolute stereochemistry.
 Double bond geometry as shown.



● HCl

RN 221549-92-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



● HCl

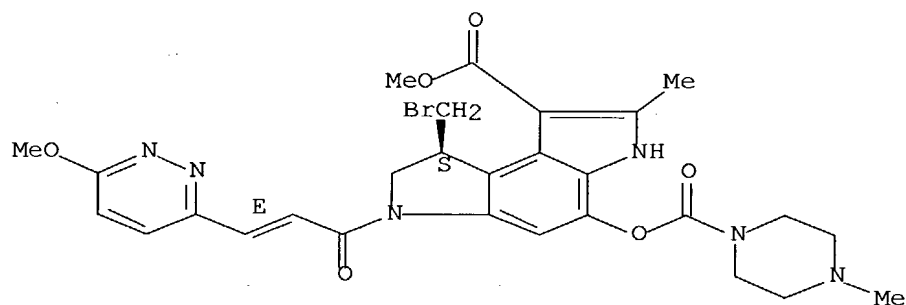
RN 221549-95-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-

4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



● HCl

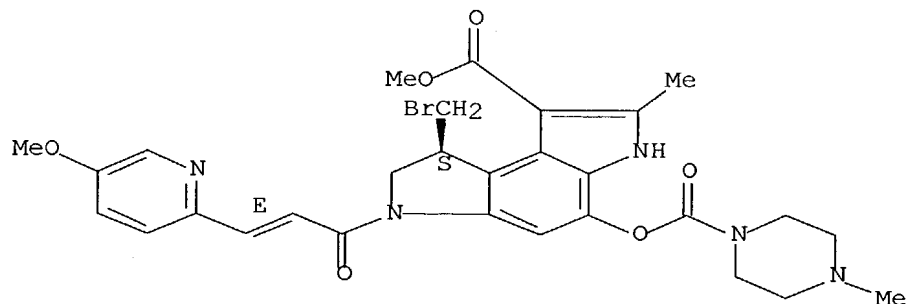
RN 221549-99-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-

4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



● HCl

IT 221549-88-8P 221549-91-3P 221549-94-6P
221549-98-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(synthesis and antitumor activity of β -heteroarylacryloyl group
bearing pyrrole analogs of duocarmycin)

RN 221549-88-8 CAPLUS

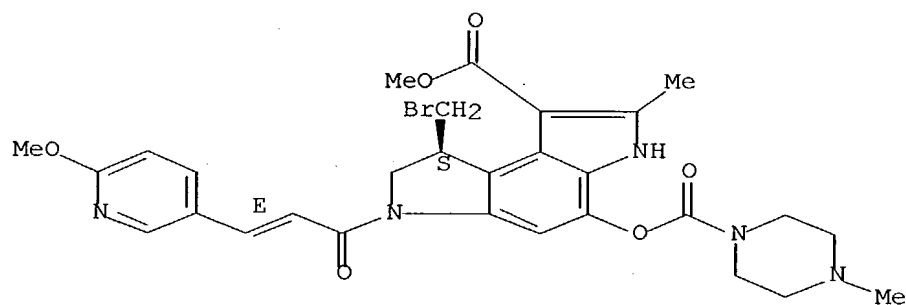
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-

4-

[[(4-methyl-1-piperazinyl)carbonyloxy]-, methyl ester, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 221549-91-3 CAPLUS

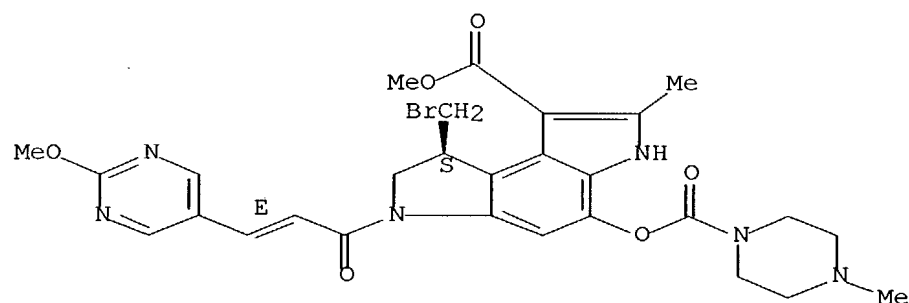
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-
methyl-

4-[[(4-methyl-1-piperazinyl)carbonyloxy]-, methyl ester, (8S)- (9CI)

(CA

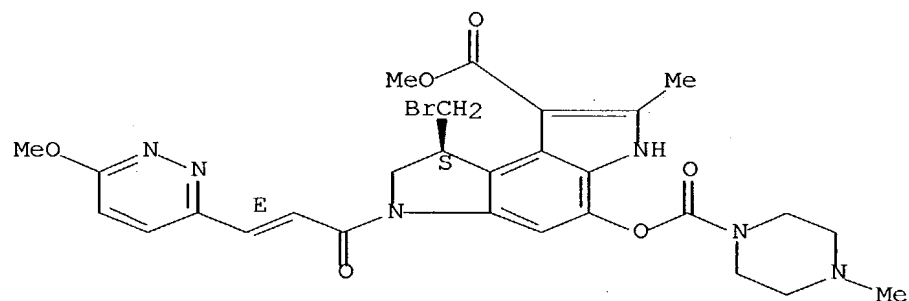
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



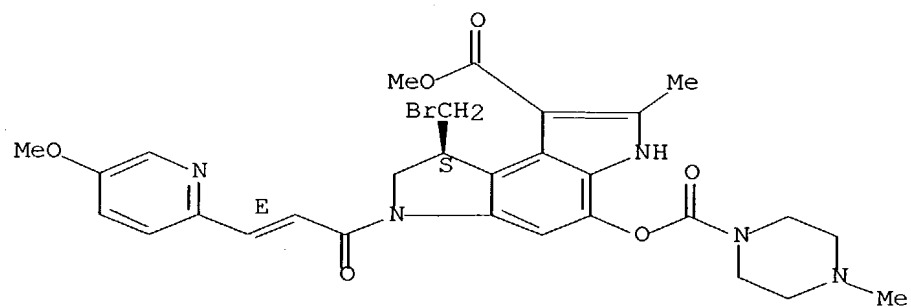
RN 221549-94-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



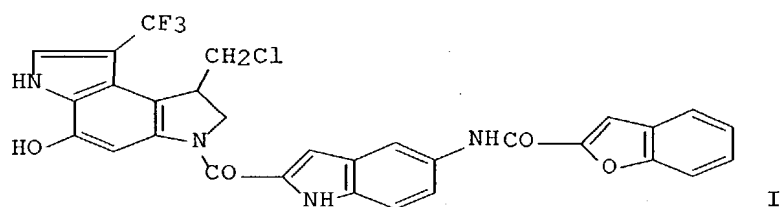
RN 221549-98-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 37 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:32649 CAPLUS Full-text
 DN 130:168271
 TI Synthesis and cytotoxicity of various structural types of novel
 cyclopropapyrroloindole (CPI) derivatives
 AU Fukuda, Yasumichi; Furuta, Hirosuke; Kusama, Yoshie; Ebisu, Hiroyuki;
 Oomori, Yasuo; Terashima, Shiro
 CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd, Nogi,
 Tochigi, 329-0114, Japan
 SO Heterocycles (1998), 49, 53-58
 CODEN: HTCYAM; ISSN: 0385-5414
 PB Japan Institute of Heterocyclic Chemistry
 DT Journal
 LA English
 GI



AB Various structural types of novel cyclopropapyrroloindole (CPI) derivs.,
 e.g. I, were synthesized and their cytotoxicity was evaluated.

IT **176685-39-5**

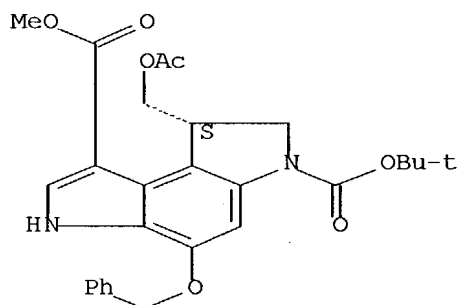
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and antitumor activity of cyclopropapyrroloindole
 derivs.)

RN 176685-39-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-
 dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 176685-35-1P 176685-36-2P 176685-40-8P
176685-41-9P 176685-42-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and antitumor activity of cyclopropapyrroloindole
derivs.)

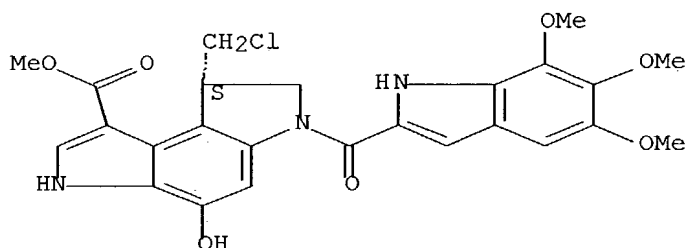
RN 176685-35-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
methyl

ester, (8S)- (9CI) (CA INDEX NAME)

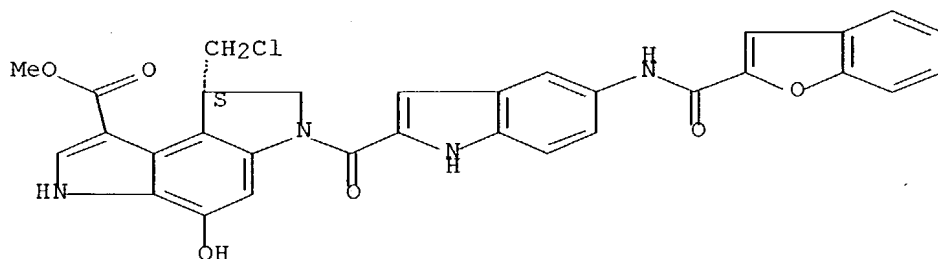
Absolute stereochemistry. Rotation (-).



RN 176685-36-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

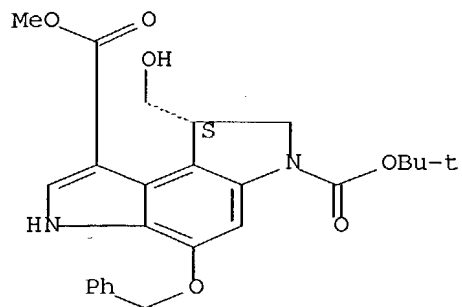
Absolute stereochemistry. Rotation (+).



RN 176685-40-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

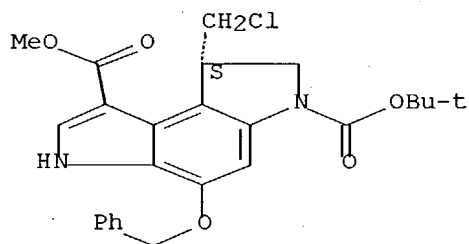
Absolute stereochemistry. Rotation (-).



RN 176685-41-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

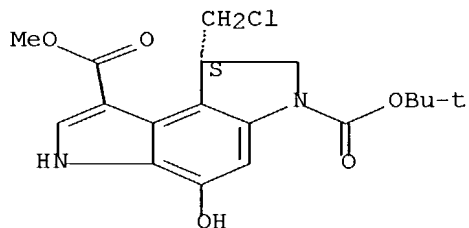
Absolute stereochemistry. Rotation (-).



RN 176685-42-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 1-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 38 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:789131 CAPLUS Full-text
 DN 130:24911
 TI syntheses and cytotoxicities of analogs of duocarmycin and CC-1065
 IN Boger, Dale L.
 PA The Scripps Research Institute, USA
 SO PCT Int. Appl., 115 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9852925	A1	19981126	WO 1998-US10535	19980522
	W:				
	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9876927	A1	19981211	AU 1998-76927	19980522
	AU 754083	B2	20021107		
	EP 983248	A1	20000308	EP 1998-924851	19980522
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002503228	T2	20020129	JP 1998-550697	19980522
	NZ 500789	A	20020531	NZ 1998-500789	19980522
	US 6281354	B1	20010828	US 1999-423576	19991109
PRAI	US 1997-48505P	P	19970522		
	WO 1998-US10535	W	19980522		

OS MARPAT 130:24911

AB Syntheses of analogs and derivs. of duocarmycin and CC-1065 are provided. Tabulations of their activities as antitumor antibiotics and as cell toxicity agents are presented as well as their sequences specific DNA alkylating activities.

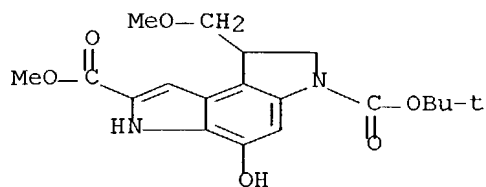
IT **216298-39-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses) (syntheses, DNA alkylating, antitumor antibiotic and cytotoxicities of analogs of duocarmycin and CC-1065)

RN 216298-39-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-4-hydroxy-8-(methoxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



IT **144786-07-2**

RL: RCT (Reactant); RACT (Reactant or reagent)

(syntheses, DNA alkylating, antitumor antibiotic and cytotoxicities

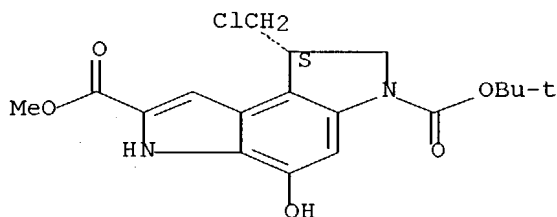
of

analogs of duocarmycin and CC-1065)

RN 144786-07-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **182957-20-6P 182957-21-7P 182957-22-8P**
182957-23-9P 182957-24-0P 190060-24-3P
190060-25-4P 190060-26-5P 190060-27-6P
190060-28-7P 190060-35-6P 190060-36-7P
190060-38-9P 190060-39-0P 190060-40-3P
190060-42-5P 190060-43-6P 190060-44-7P
190322-73-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(syntheses, DNA alkylating, antitumor antibiotic and cytotoxicities

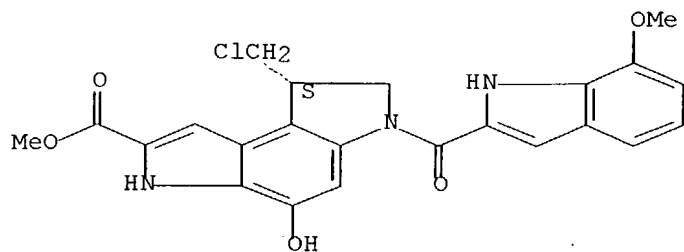
of

analogs of duocarmycin and CC-1065)

RN 182957-20-6 CAPLUS

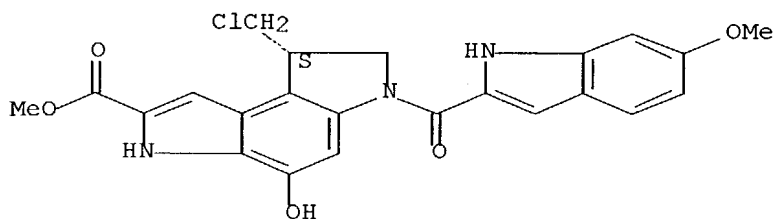
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(7-methoxy-1H-indol-2-yl)carbonyl]-, methyl
ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



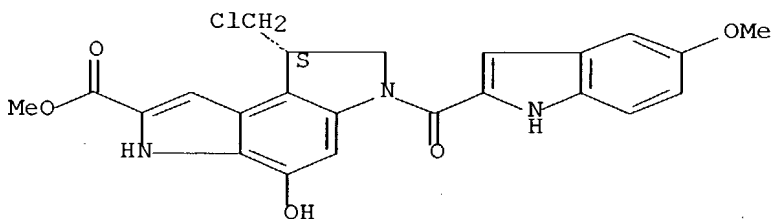
RN 182957-21-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(6-methoxy-1H-indol-2-yl)carbonyl]-, methyl
 ester,
 (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 182957-22-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-, methyl
 ester,
 (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

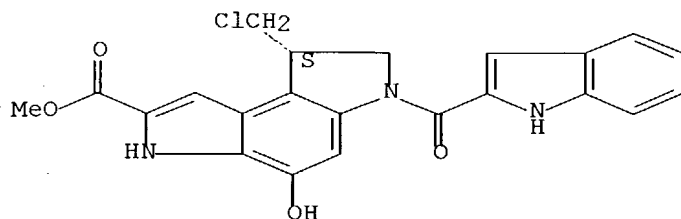


RN 182957-23-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-

tetrahydro-4-hydroxy-6-(1H-indol-2-ylcarbonyl)-, methyl ester, (8S)-
(9CI)

(CA INDEX NAME)

Absolute stereochemistry.

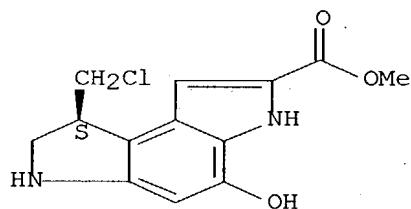


RN 182957-24-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-hydroxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



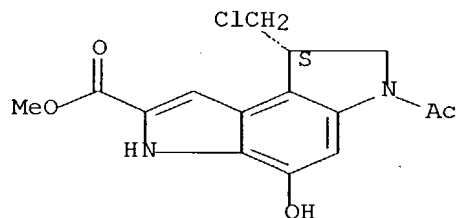
● HCl

RN 190060-24-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-8-
(chloromethyl)-

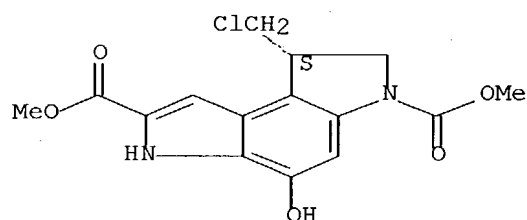
3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry. Rotation (-).



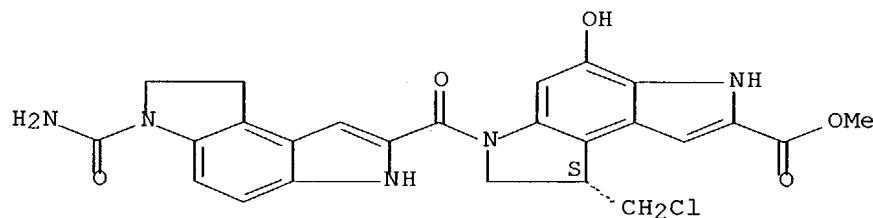
RN 190060-25-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, dimethyl ester, (8S)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 190060-26-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[6-(aminocarbonyl)-
 3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-
 (chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI)
 (CA INDEX NAME)

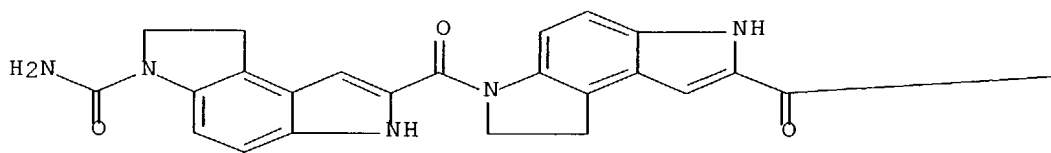
Absolute stereochemistry. Rotation (+).



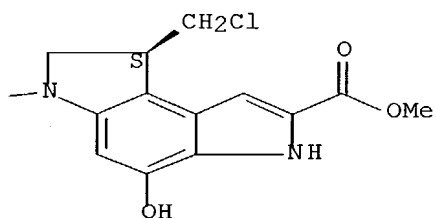
RN 190060-27-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[6-[[6-
 (aminocarbonyl)-
 3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-
 tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-(chloromethyl)-
 3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A

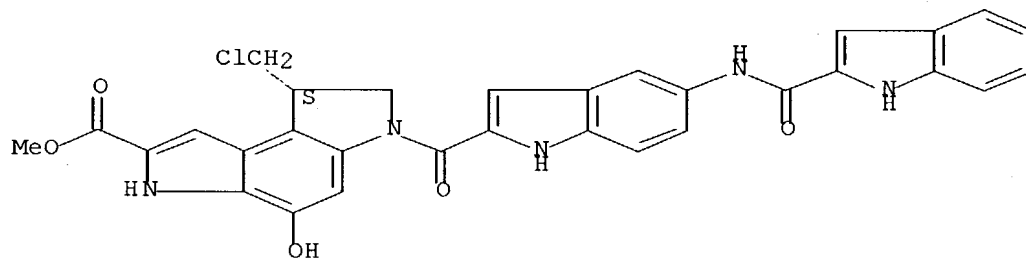


PAGE 1-B



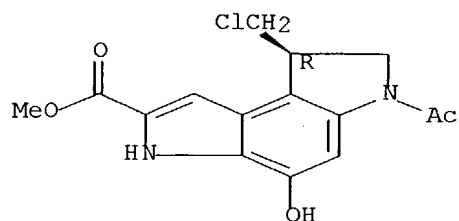
RN 190060-28-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-
yl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



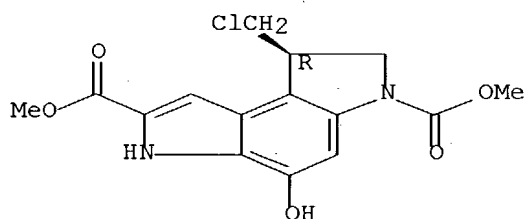
RN 190060-35-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-8-
(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8R)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry. Rotation (+).



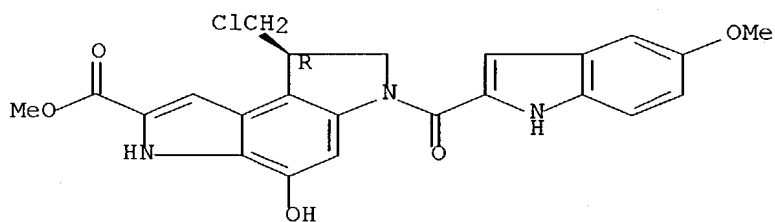
RN 190060-36-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, dimethyl ester, (8R)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 190060-38-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-, methyl
 ester,
 (8R)- (9CI) (CA INDEX NAME)

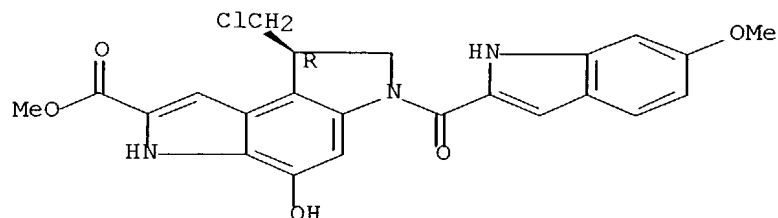
Absolute stereochemistry. Rotation (-).



RN 190060-39-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(6-methoxy-1H-indol-2-yl)carbonyl]-, methyl
 ester,

(8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

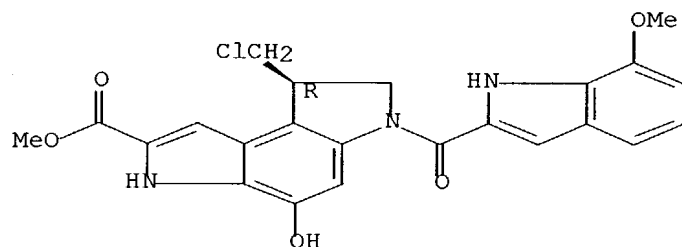


RN 190060-40-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(7-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,

(8R)- (9CI) (CA INDEX NAME)

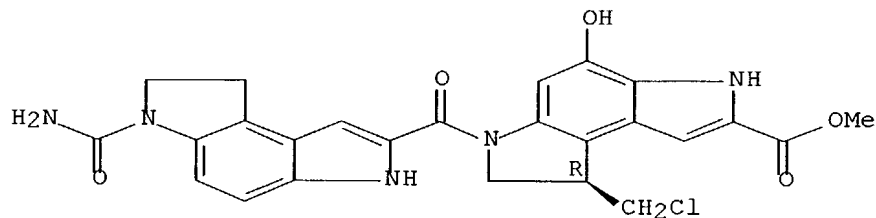
Absolute stereochemistry. Rotation (+).



RN 190060-42-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[6-(aminocarbonyl)-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

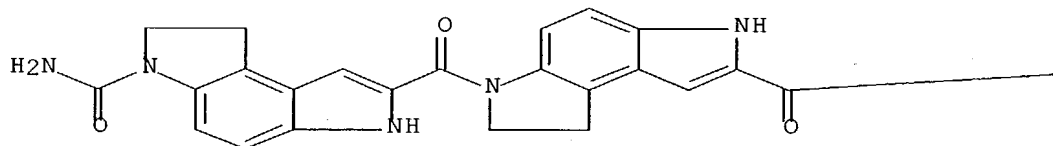


RN 190060-43-6 CAPLUS

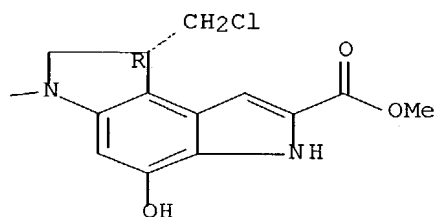
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[[(8R)-6-[[6-(aminocarbonyl)-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



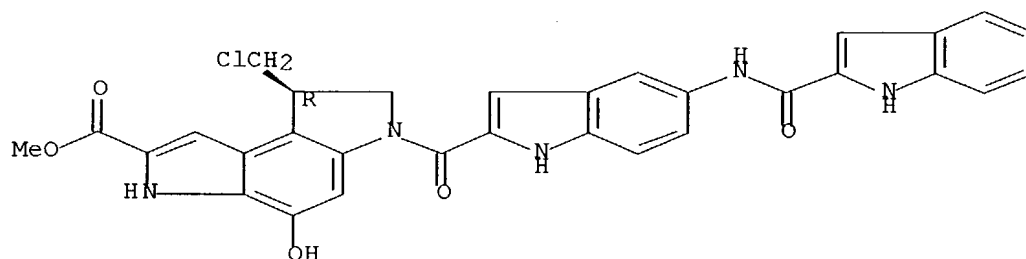
PAGE 1-B



RN 190060-44-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

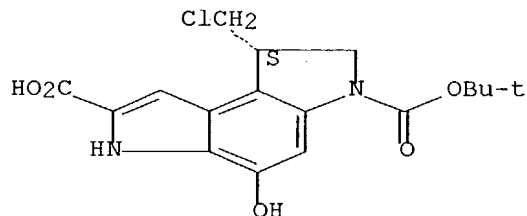
Absolute stereochemistry. Rotation (-).



RN 190322-73-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 181417-69-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(syntheses, DNA alkylating, antitumor antibiotic and cytotoxicities

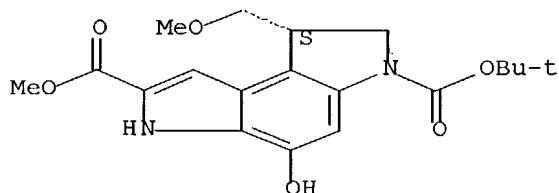
of

analogs of duocarmycin and CC-1065)

RN 181417-69-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
7,8-dihydro-4-hydroxy-8-(methoxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 39 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:674015 CAPLUS Full-text

DN 130:75837

TI Phase I study of the duocarmycin semisynthetic derivative KW-2189 given daily for five days every six weeks

AU Alberts, Steven R.; Erlichman, Charles; Reid, Joel M.; Sloan, Jeff A.; Ames, Matthew M.; Richardson, Ronald L.; Goldberg, Richard M.

CS Divisions of Medical Oncology, Mayo Clinic, Rochester, MN, 55905, USA

SO Clinical Cancer Research (1998), 4(9), 2111-2117

CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

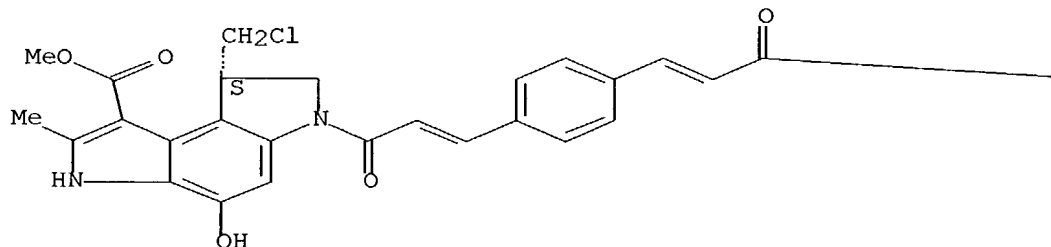
AB The duocarmycins represent a new group of antitumor antibiotics produced by Streptomyces that bind to the minor groove of DNA. KW-2189 is a water-soluble semisynthetic derivative of duocarmycin B2, with significant activity in murine and human tumor models. We conducted a Phase I trial of KW-2189 in patients who had solid tumors that were refractory to standard chemotherapy or for whom no more effective therapy existed. KW-2189 was administered as a rapid i.v. bolus daily for 5 days every 6 wk. Twenty-two patients were enrolled and received a total of 31 cycles of KW-2189. Leukopenia, neutropenia, and thrombocytopenia were the dose-limiting toxicities, with nadirs occurring at medians of 36, 38, and 29 days, resp., at the 0.04 mg/m2/day dose level. Nonhematol. toxicities were mild, although one patient developed grade 3 fatigue. Four patients had stable disease over two to four cycles of treatment and showed no cumulative toxicity. The mean t1/2, plasma clearance, and steady-state volume of distribution were 13.5 min, 1,287 mL/min/m2, and 10,638 mL/m2, resp. Pharmacokinetics were similar on days 1 and 5, with no drug accumulation in plasma. The active metabolite DU-86 was not consistently found in patient plasma. For Phase II trials, when the 5 days every 6 wk schedule was used, 0.04 mg/m2/day KW-2189 appears to be the maximal tolerated dose, especially for patients who have received prior chemotherapy. At this dose level, the drug was well tolerated, and the toxicities were acceptable.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

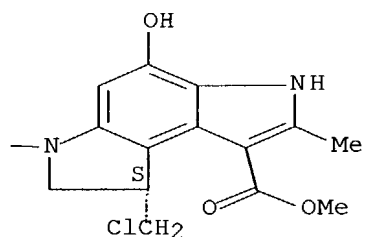
L10 ANSWER 40 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:554714 CAPLUS Full-text
 DN 129:254358
 TI The novel cyclopropapyrroloindole (CPI) bisalkylators bearing
 3,3'-(1,4-phenylene)diacryloyl group as a linker
 AU Fukuda, Yasumichi; Seto, Shigeki; Furuta, Hirosuke; Ebisu, Hiroyuki;
 Oomori, Yasuo; Terashima, Shiro
 CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Tochigi,
 329-0114, Japan
 SO Bioorganic & Medicinal Chemistry Letters (1998), 8(15), 2003-2004
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 AB The novel cyclopropapyrroloindole (CPI) bisalkylators were synthesized
 and their antitumor activity was evaluated. Among these derivs., AT-760
 in which the two 3-methoxycarbonyl-2-trifluoromethyl-CPI (MCTFCPI)
 moieties are connected with a 3,3'-(1,4-phenylene)diacryloyl group, was
 found to exhibit more prominent cytotoxicity and antitumor activity than
 U-77779 (bizelesin).
 IT **179693-64-2P 179693-67-5P 179693-68-6P**
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); PRP (Properties); SPN (Synthetic preparation);
 BIOL
 (Biological study); PREP (Preparation)
 (preparation and antitumor activity of cyclopropapyrroloindole
 bisalkylators
 bearing 3,3'-(1,4-phenylene)diacryloyl group as linker)
 RN 179693-64-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-
 phenylenebis(1-
 oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-
 hydroxy-
 2-methyl-, dimethyl ester, (8S,8'S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

PAGE 1-A



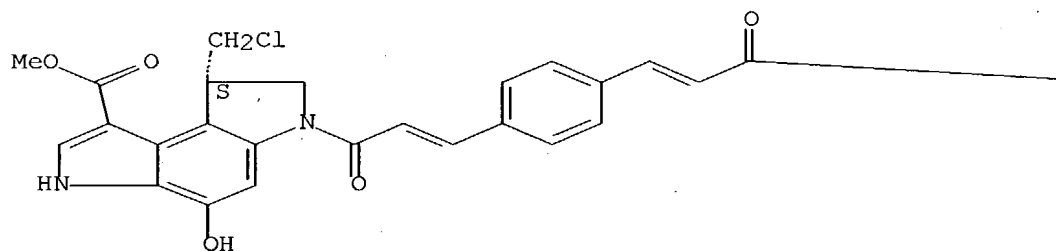
PAGE 1-B



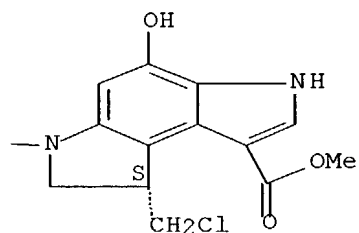
RN 179693-67-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



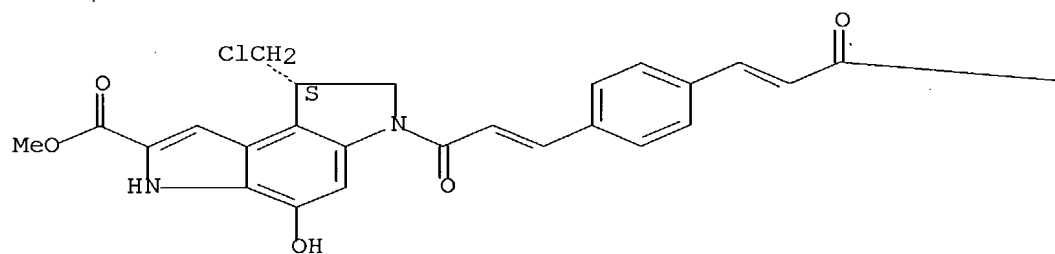
PAGE 1-B



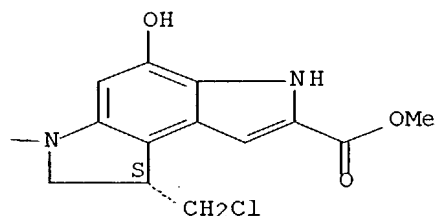
RN 179693-68-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6,6'-[1,4-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



IT 179693-47-1P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

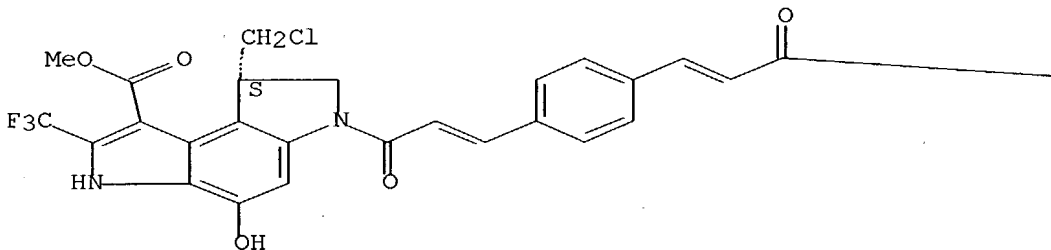
(preparation and antitumor activity of cyclopropapyrroloindole
 bisalkylators

bearing 3,3'-(1,4-phenylene)diacryloyl group as linker)

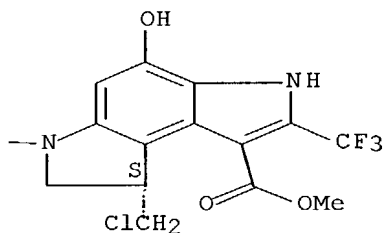
RN 179693-47-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



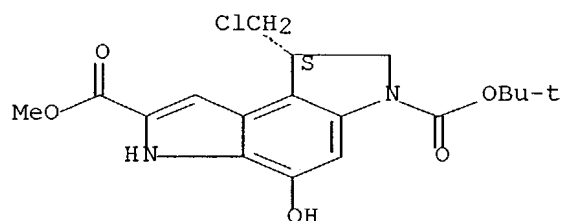
IT 144786-07-2 157904-28-4 176685-42-0
179693-97-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor activity of cyclopropapyrroloindole
bisalkylators
bearing 3,3'-(1,4-phenylene)diacryloyl group as linker)

RN 144786-07-2 CAPLUS

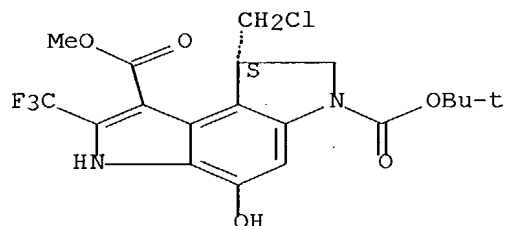
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



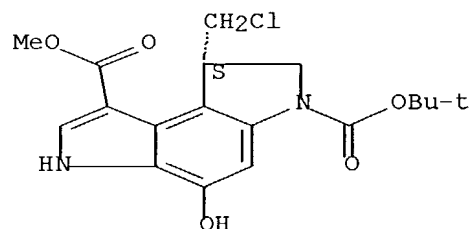
RN 157904-28-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



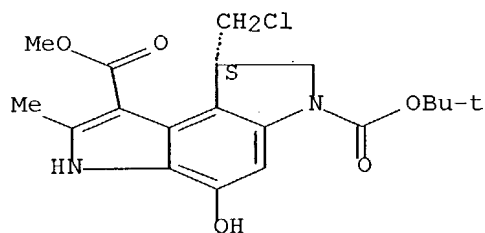
RN 176685-42-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 1-methyl
 ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 179693-97-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-methyl-, 6-(1,1-dimethylethyl)
 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 182957-24-0P 213628-70-7P 213628-71-8P
213628-72-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and antitumor activity of cyclopropapyrroloindole
bisalkylators

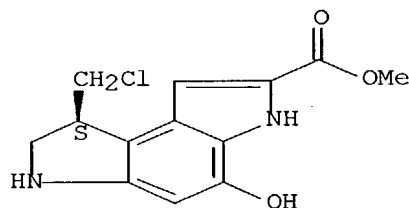
bearing 3,3'-(1,4-phenylene)diacryloyl group as linker)

RN 182957-24-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-hydroxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



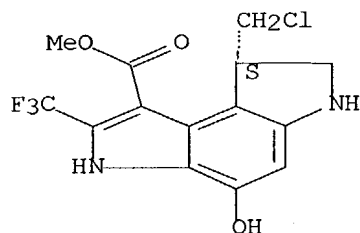
● HCl

RN 213628-70-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester,
monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

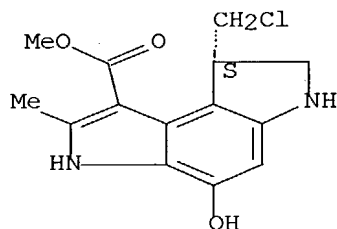
Absolute stereochemistry.



● HCl

RN 213628-71-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-methyl-, methyl ester, monohydrochloride, (8S)-
 (9CI) (CA INDEX NAME)

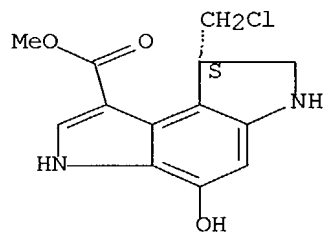
Absolute stereochemistry.



● HCl

RN 213628-72-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
 INDEX NAME)

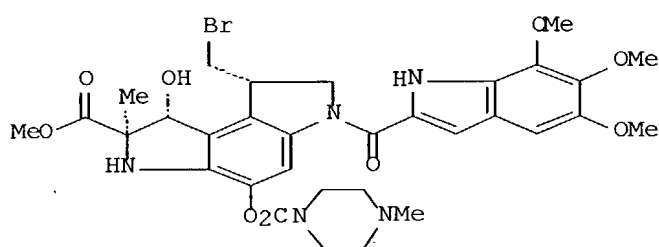
Absolute stereochemistry.



● HCl

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 41 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:536379 CAPLUS Full-text
 DN 129:302469
 TI Practical Synthesis of the High-Quality Antitumor Agent KW-2189 from
 Duocarmycin B2 Using a Facile One-Pot Synthesis of an Intermediate
 AU Kinugawa, Masahiko; Nagamura, Satoru; Sakaguchi, Akihiko; Masuda,
 Yoshiaki; Saito, Hiromitsu; Ogasa, Takehiro; Kasai, Masaji
 CS Sakai Research Laboratories, Kyowa Hakko Kogyo Co., Osaka, 590, Japan
 SO Organic Process Research & Development (1998), 2(6), 344-350
 CODEN: OPRDFK; ISSN: 1083-6160
 PB American Chemical Society
 DT Journal
 LA English
 GI



I

AB A facile and large-scale preparation process of a potent antitumor agent
 KW-2189, derived from the antitumor antibiotic duocarmycin B2, has been
 developed. This new synthetic route required three steps: (i) one-pot
 carbamoylation and subsequent reduction, (ii) Wagner-Meerwein
 rearrangement of the methoxycarbonyl group for the production of the
 pyrrole compound, and (iii) formation of the hydrobromide salt. The key
 strategic improvement was to obtain good quality hydroxy compound I in a
 reasonable yield without isolation of the unstable keto intermediate.
 During com.-scale production at a scale of about 50 g, this strategy
 provided high-quality KW-2189 in a 55% overall yield from duocarmycin
 B2. Potential degradation compds. were also synthesized and shown to be
 absent in the KW-2189 prepared

IT **124325-94-6**, Duocarmycin B2

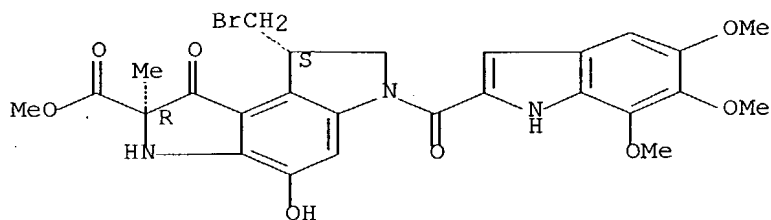
RL: RCT (Reactant); RACT (Reactant or reagent)

(practical synthesis of high-quality antitumor agent KW-2189 from
 duocarmycin B2 using a facile one-pot synthesis of intermediate)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
 indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154901-65-2P 160819-29-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

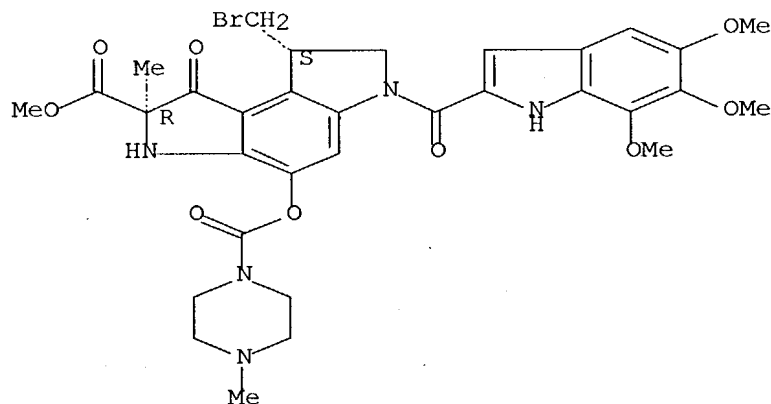
(practical synthesis of high-quality antitumor agent KW-2189 from duocarmycin B2 using a facile one-pot synthesis of intermediate)

RN 154901-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (2R,8S)-

(9CI) (CA INDEX NAME)

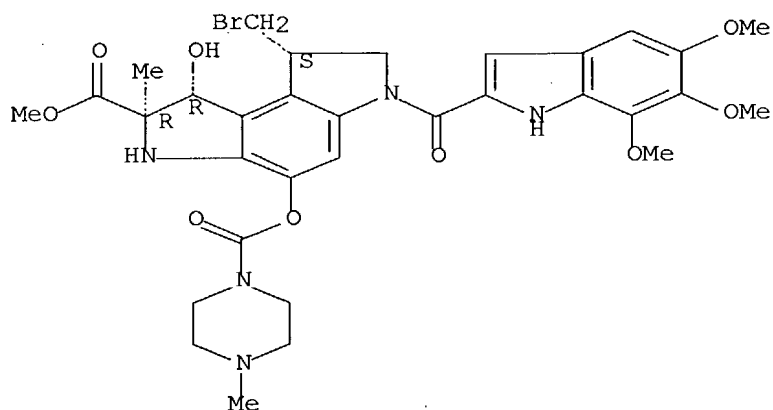
Absolute stereochemistry.



RN 160819-29-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154889-68-6P 160819-28-3P 171599-29-4P
214051-54-4P

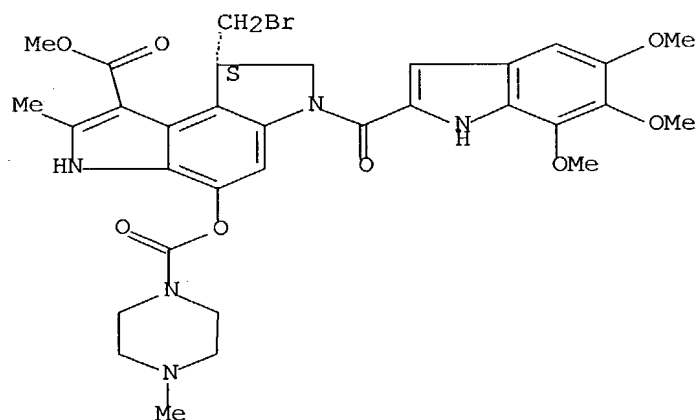
RL: SPN (Synthetic preparation); PREP (Preparation)
(practical synthesis of high-quality antitumor agent KW-2189 from
duocarmycin B2 using a facile one-pot synthesis of intermediate)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)-(9CI) (CA

INDEX
NAME)

Absolute stereochemistry.



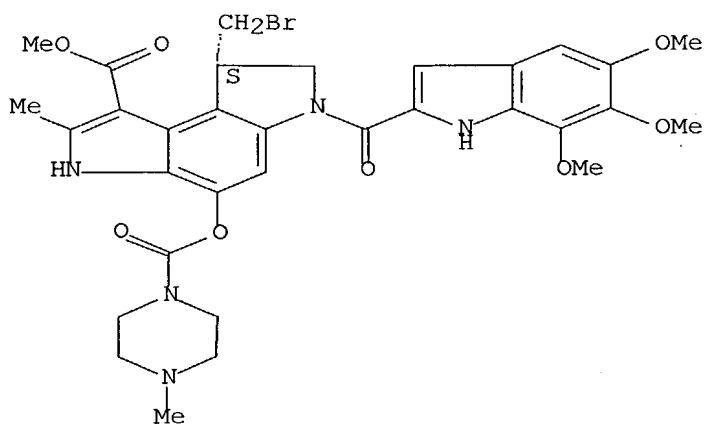
RN 160819-28-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,

(8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

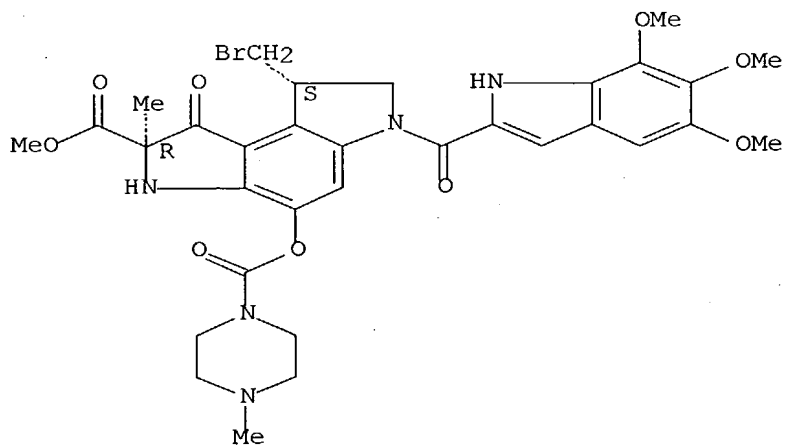
● HBr

RN 171599-29-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-
piperazinyl) carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester,
monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

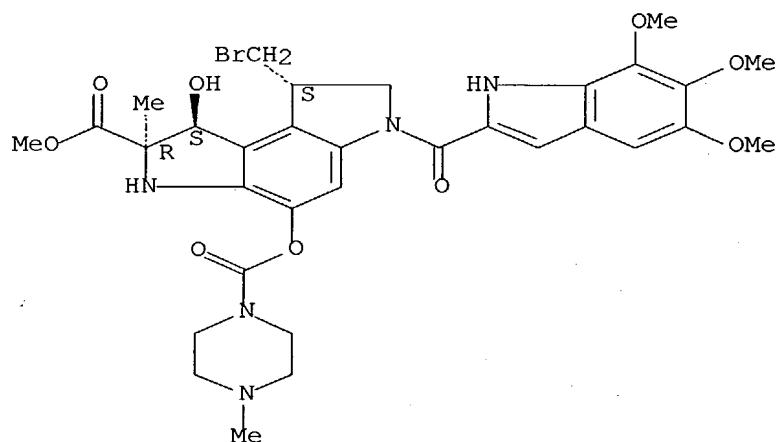


● HCl

RN 214051-54-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[(4-methyl-1-
 piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl ester, (1S,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 42 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:527333 CAPLUS Full-text
 DN 129:161451
 TI Preparation of antitumor and antimicrobial pyrroloindole derivatives and their intermediates.
 IN Fukuda, Yasumichi; Shimazawa, Rumiko; Oomori, Yasuo; Terashima, Shiro
 PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center
 SO PCT Int. Appl., 32 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9832757	A1	19980730	WO 1998-JP234	19980122
	W:			AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ,	
TM				RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG	
	JP 10265473	A2	19981006	JP 1998-7211	19980119
	AU 9855760	A1	19980818	AU 1998-55760	19980122
	EP 972775	A1	20000119	EP 1998-900695	19980122
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,	
FI	TW 491846	B	20020621	TW 1998-87101164	19980123
	US 6080859	A	20000627	US 1999-341872	19990719
PRAI	JP 1997-11289	A	19970124		
	JP 1998-7211	A	19980119		
	WO 1998-JP234	W	19980122		
OS	MARPAT 129:161451				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = OH, pyrrolidinyl; n = 1, 2; R2 = lower (C1-4) alkyl; Y-Y or Y-X = CH2, CHOH, CH2-CH2, O-CH2 or NMe-CH2; Z1 = Cl or Br; and Ar1 = Q-Q4; Z2, Z3 = O, NH; m = 1-4 integer; and Ar2 = Q-Q3 above] are prepared Thus, II [R = H] was reacted with (2S)-pyrrolidine-2-methanol in THF containing 4-nitrophenyl chloroformate and Et3N to give II [R = (S)-2-(hydroxymethyl)pyrrolidin-1-ylcarbonyl]. In an in vitro study using female mice II [R = 2-(hydroxymethyl)piperidinocarbonyl] (also prepared) at 1.0 mg/Kg s.c. showed ca. 99% inhibition of the growth of adriamycin-resistant strain of M5076 cells. The stability of I was also studied.

IT 211053-32-6P 211053-33-7P 211053-34-8P
 211053-35-9P 211053-36-0P 211053-37-1P
 211053-38-2P 211053-39-3P 211053-40-6P
 211053-41-7P 211053-42-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

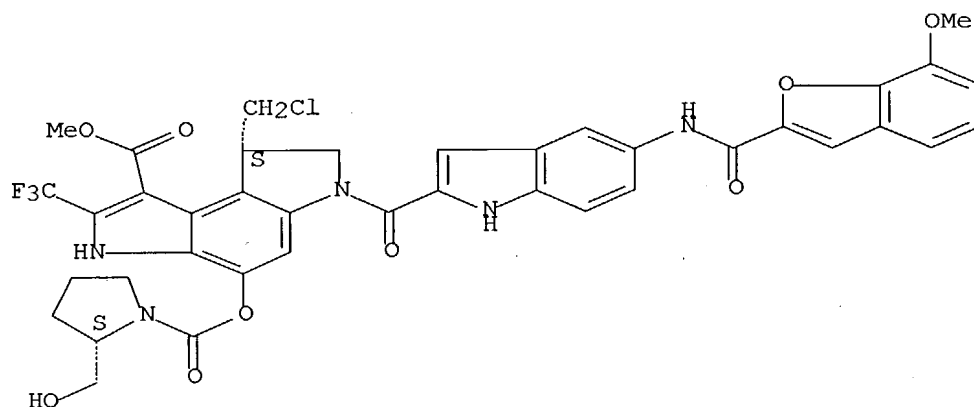
(preparation of antitumor and antimicrobial pyrroloindole derivs. and
their intermediates)

RN 211053-32-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-[[[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]carbonyl]oxy]-6-
[[5-
[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

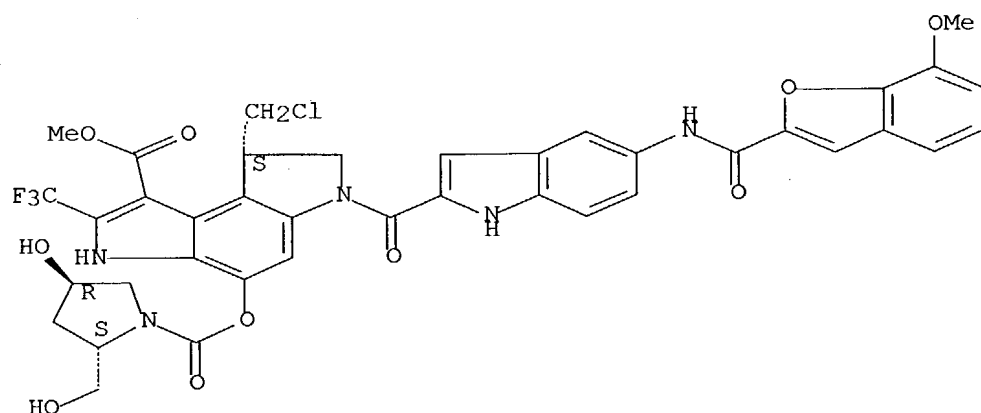


RN 211053-33-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-[[[(2S,4R)-4-hydroxy-2-(hydroxymethyl)-1-
pyrrolidinyl]carbonyl]oxy]-6-[[5-[[[(7-methoxy-2-
benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
(trifluoromethyl)-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

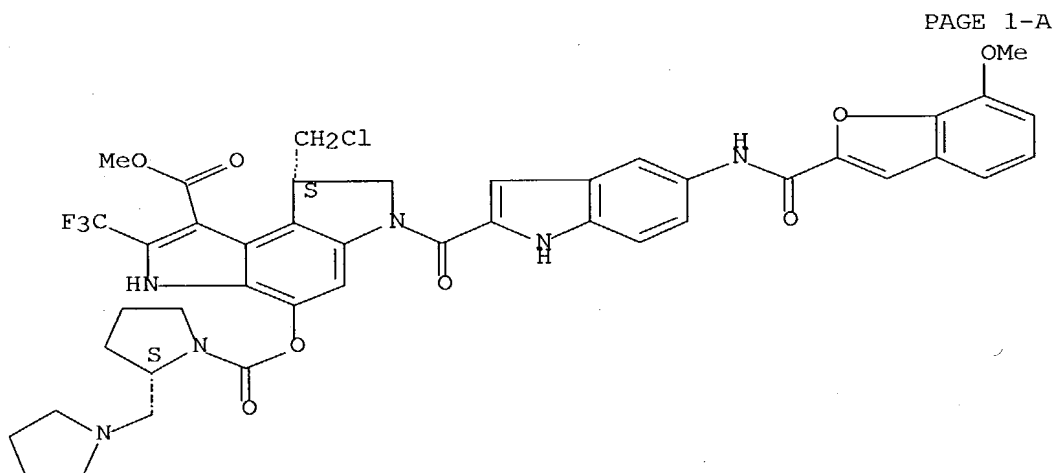


RN 211053-34-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

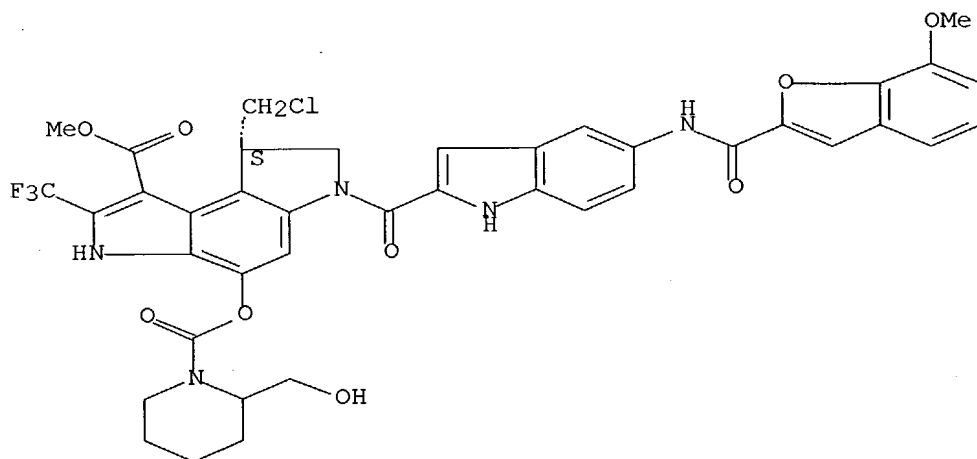


PAGE 2-A

● HCl

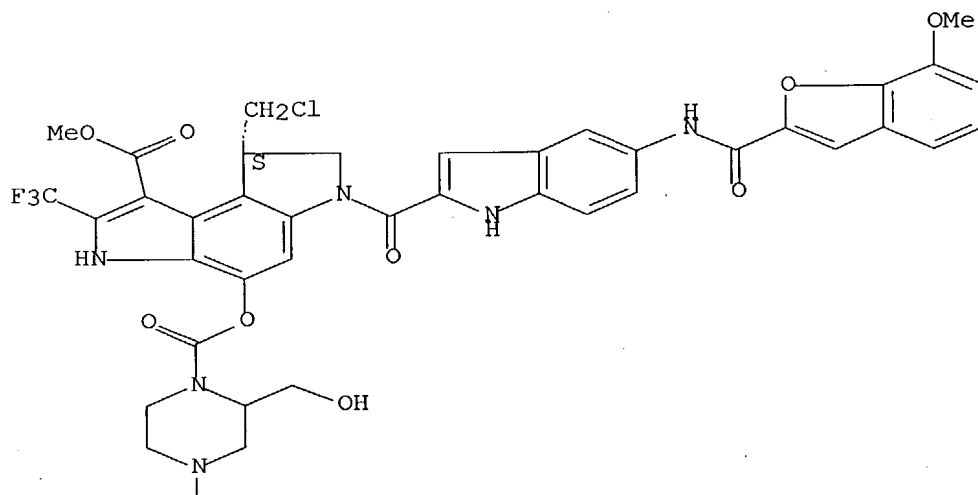
RN 211053-35-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[2-(hydroxymethyl)-1-piperidinyl]carbonyl]oxy]-6-[[5-
 [[(7-
 methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 211053-36-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[2-(hydroxymethyl)-4-methyl-1-piperazinyl]carbonyl]oxy]-
 6-
 [[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-
 2-
 (trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

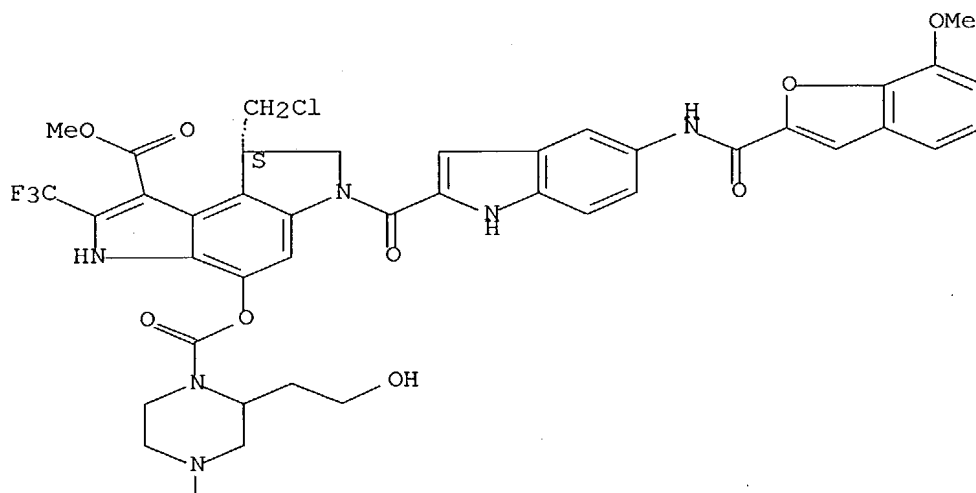


Me

● HCl

RN 211053-37-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[2-(2-hydroxyethyl)-4-methyl-1-piperazinyl]carbonyl]oxy]-
 6-
 [[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-
 2-
 (trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

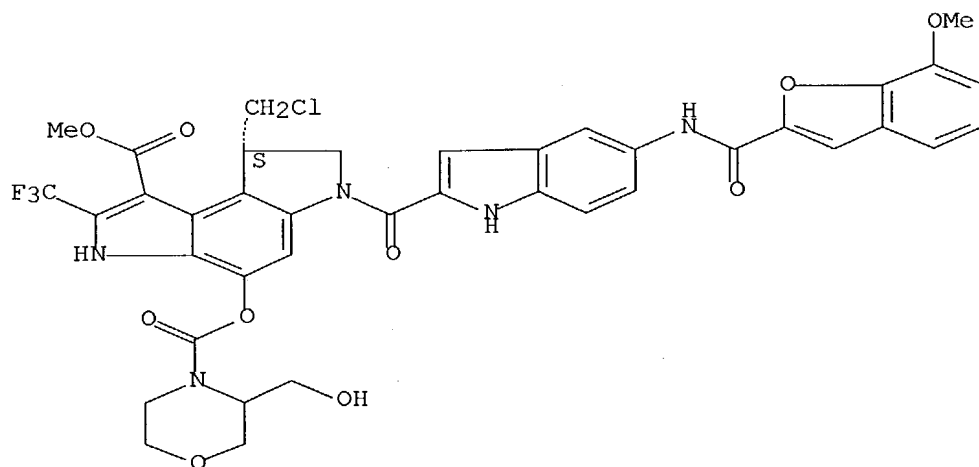


Me

● HCl

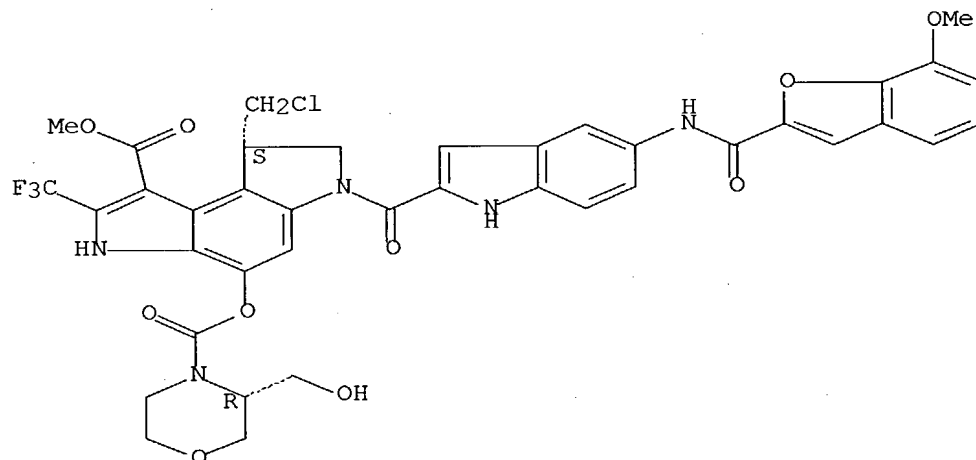
RN 211053-38-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-[[5-
 [[(7-
 methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



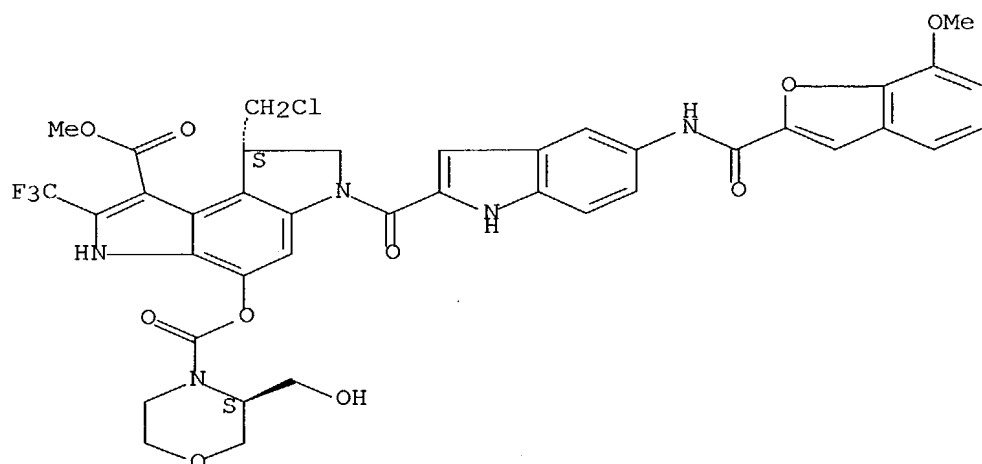
RN 211053-39-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[(3R)-3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-
 [[5-
 [[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



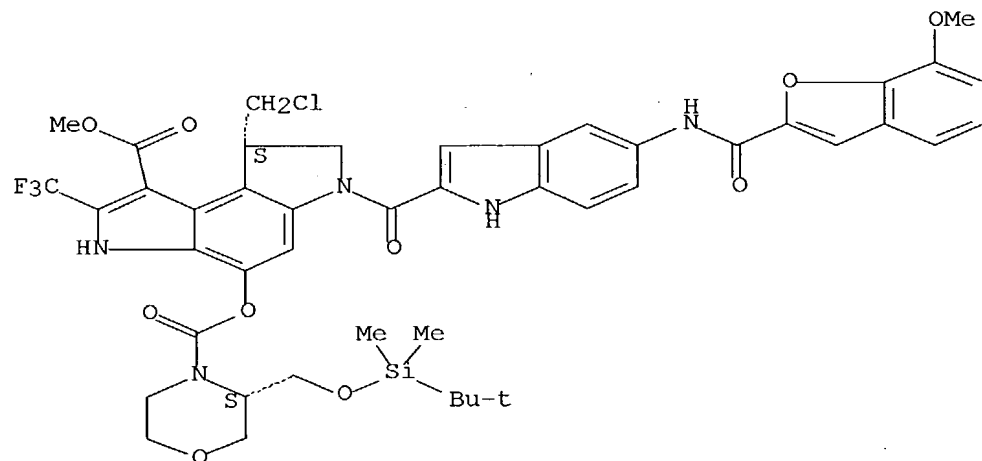
RN 211053-40-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[(3S)-3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-
 [[5-
 [[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 211053-41-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(3S)-
 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-
 morpholinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[7-methoxy-2-
 benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-,
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

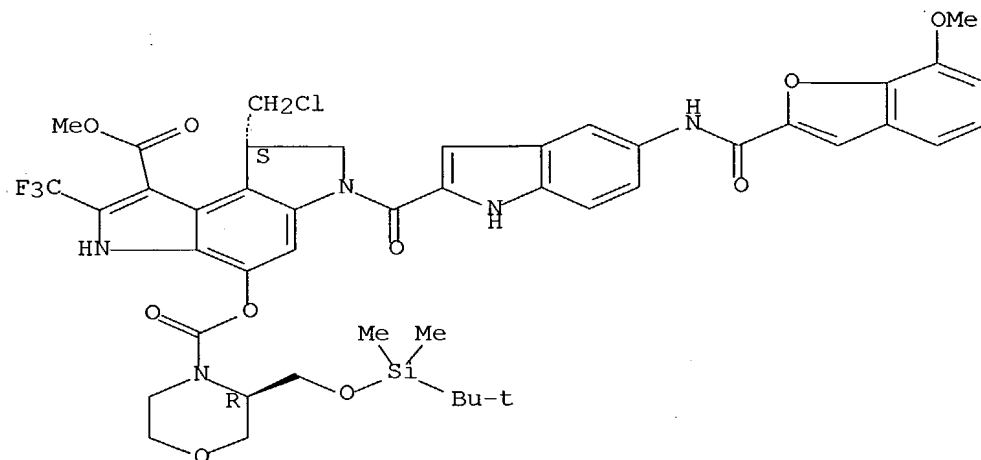
Absolute stereochemistry.



RN 211053-42-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[[(3R)-
 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-
 morpholinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[(7-methoxy-2-
 benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-,
 methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



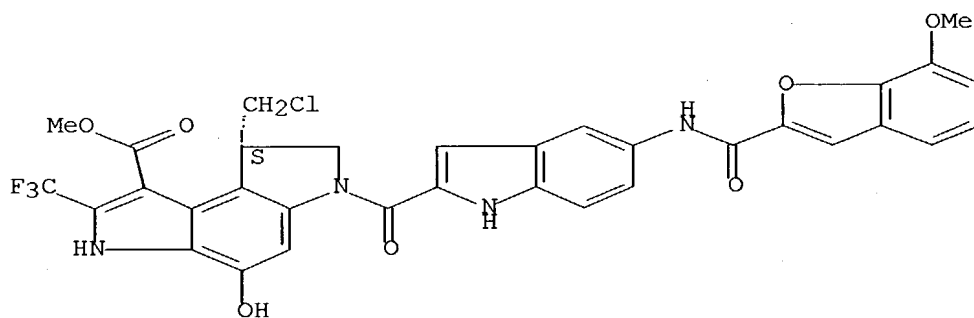
IT 157904-32-0

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of antitumor and antimicrobial pyrroloindole derivs. and
 their intermediates)

RN 157904-32-0 CAPLUS

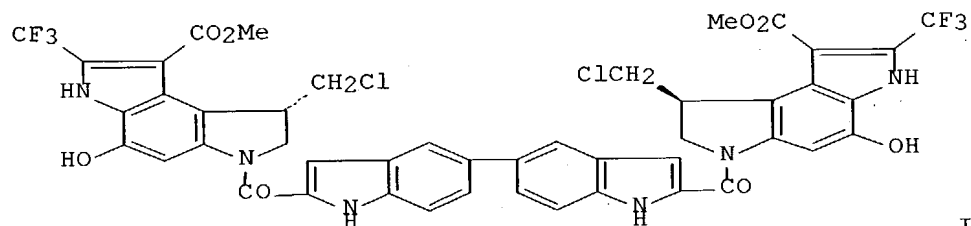
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[[(7-methoxy-2-
 benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-, methyl ester, (8S)- (9CI) (CAINDEX NAME)

Absolute stereochemistry. Rotation (+).



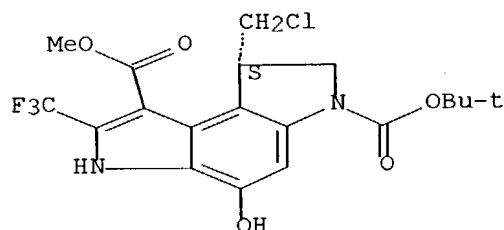
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 43 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:401968 CAPLUS Full-text
 DN 129:122589
 TI Novel cyclopropapyrroloindole (CPI) bisalkylators bearing
 methoxycarbonyl
 and trifluoromethyl groups
 AU Fukuda, Yasumichi; Furuta, Hirosuke; Kusama, Yoshie; Ebisu, Hiroyuki;
 Oomori, Yasuo; Terashima, Shiro
 CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Tochigi,
 329-0114, Japan
 SO Bioorganic & Medicinal Chemistry Letters (1998), 8(11), 1387-1390
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier Science Ltd.
 DT Journal
 LA English
 GI



AB Novel 3-(methoxycarbonyl)-2-(trifluoromethyl)cyclopropapyrroloindole
 (MCTFCPI) bisalkylators were synthesized, and their antitumor activity
 was evaluated. Among these derivs., I was found to exhibit more
 prominent cytotoxicity and antitumor activity than U-77,779 (bizelesin).
 IT **157904-28-4**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (cyclopropapyrroloindole bisalkylators bearing methoxycarbonyl and
 trifluoromethyl groups)
 RN 157904-28-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 157823-55-7P 180525-91-1P 180525-92-2P

180525-93-3P 180525-94-4P 180525-96-6P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)

(preparation and antitumor activity of)

RN 157823-55-7 CAPLUS

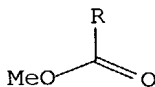
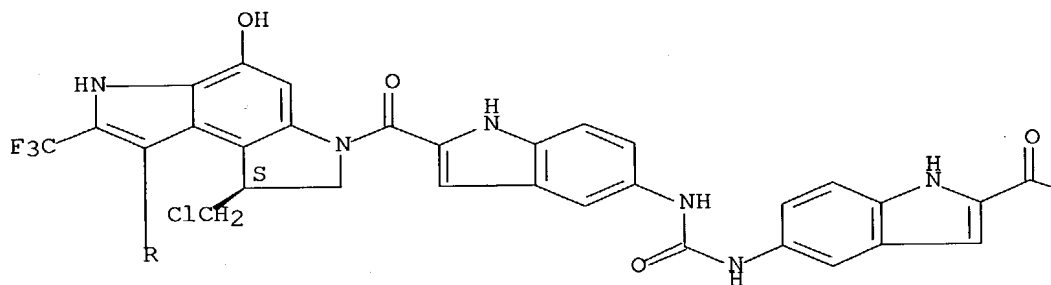
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[carbonylbis(imino-

1H-

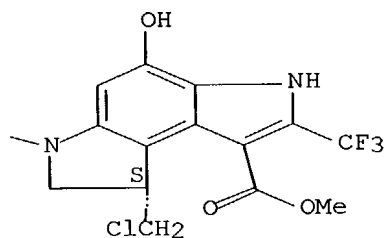
indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

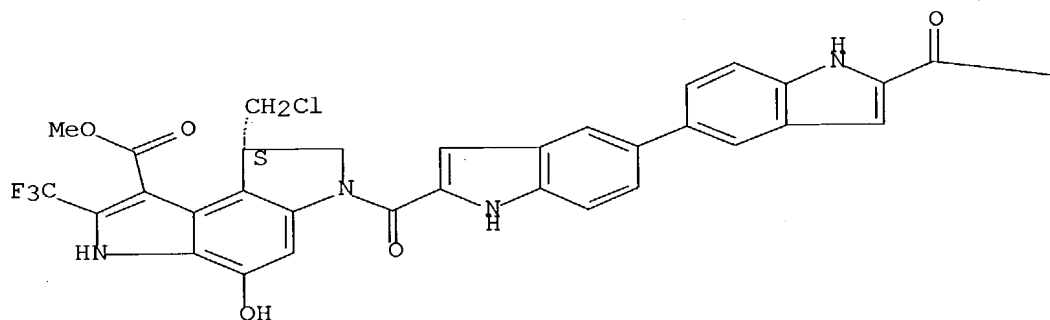


RN 180525-91-1 CAPLUS

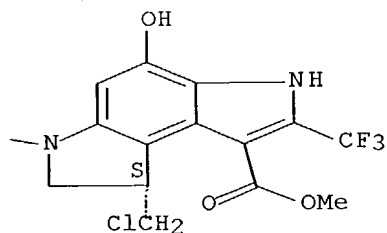
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-([5,5'-bi-1H-indole]-2,2'-diylldicarbonyl)bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

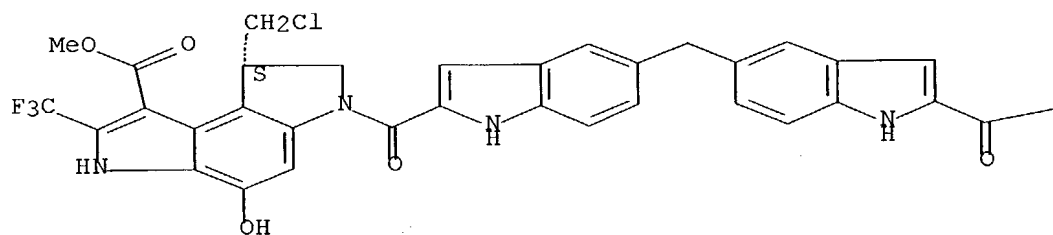


RN 180525-92-2 CAPLUS

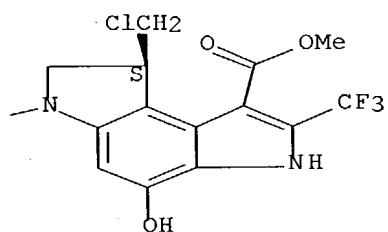
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[methylenebis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

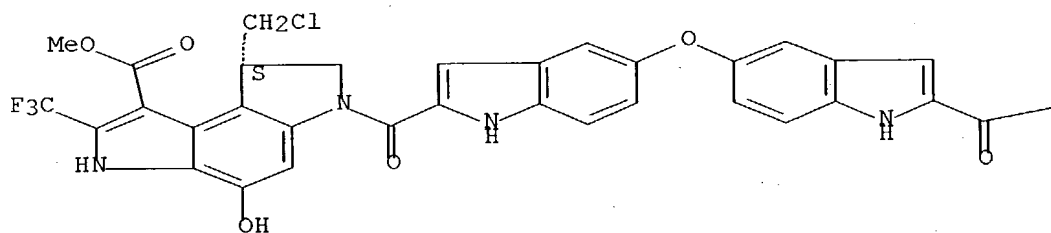


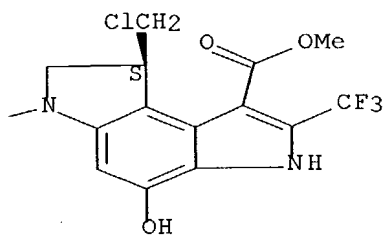
RN 180525-93-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[oxybis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A

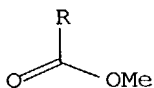
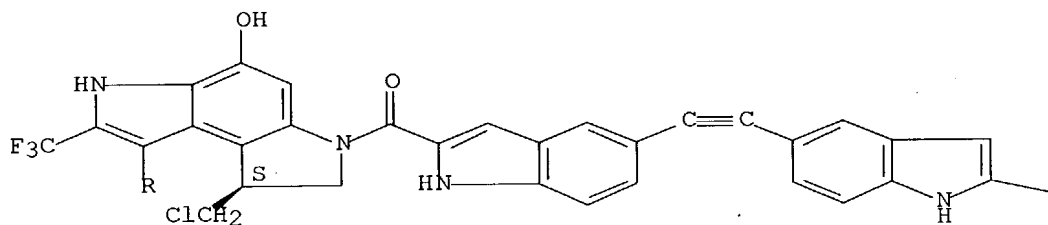


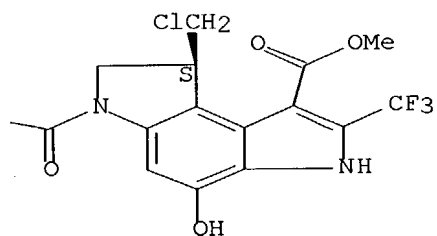


RN 180525-94-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,2-ethynediylbis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

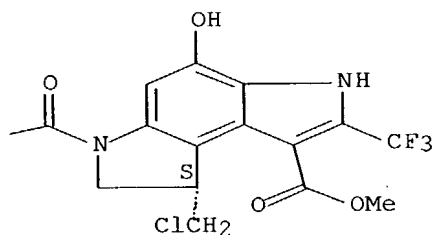
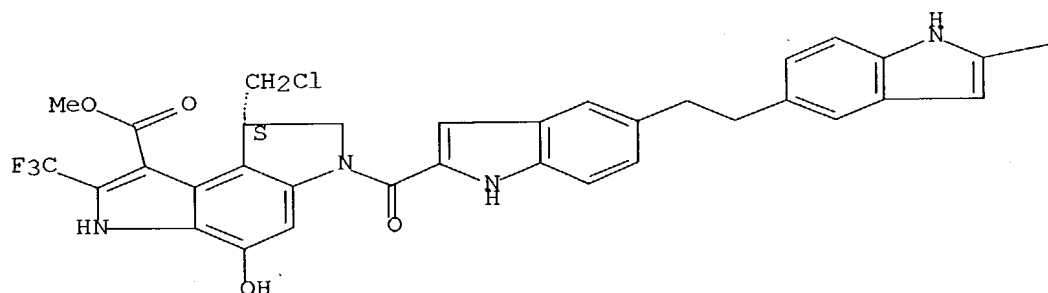
Absolute stereochemistry. Rotation (+).





RN 180525-96-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,2-ethanediylbis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 44 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:197505 CAPLUS Full-text
 DN 128:243876
 TI Intermediates for the preparation of duocarmycin SA and its derivatives thereof, and process for the production of the intermediates
 IN Fukuda, Yasumichi; Terashima, Shiro
 PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center; Fukuda, Yasumichi; Terashima, Shiro
 SO PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9812197	A1	19980326	WO 1997-JP2207	19970626
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, SG, SI, SK, TR, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	JP 10087666	A2	19980407	JP 1996-246097	19960918
	AU 9732749	A1	19980414	AU 1997-32749	19970626
	EP 937726	A1	19990825	EP 1997-928473	19970626
	EP 937726	B1	20030312		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1230960	A	19991006	CN 1997-198004	19970626
	CN 1090632	B	20020911		
	AT 234304	E	20030315	AT 1997-928473	19970626
	US 6066742	A	20000523	US 1999-254515	19990309
	KR 2000036211	A	20000626	KR 1999-702272	19990317
PRAI	JP 1996-246097	A	19960918		
	WO 1997-JP2207	W	19970626		
OS	CASREACT 128:243876; MARPAT 128:243876				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -- AVAILABLE VIA OFFLINE PRINT *

AB Indole derivs. I [R1, R2, R3 = protecting group; R4 = C1-6 alkyl, benzyl] undergo oxidative cyclization to give title compds. II. Thus, indoline III was reacted with Me-CHBr-COOMe in benzene containing 1,8-bis(dimethylamino)naphthalene to give 97% (3S)-I [R1 = BOC, R2 = acetyl, R3 = benzyl, R4 = Me], which was oxidized with MnO2 in N,N-dimethylacetamide containing p-nitrobenzoic acid and palladium acetate to give 23% the title compound (-)-(S)-II [R1-R4 same as above].

IT 144786-07-2P 197657-12-8P 197657-13-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

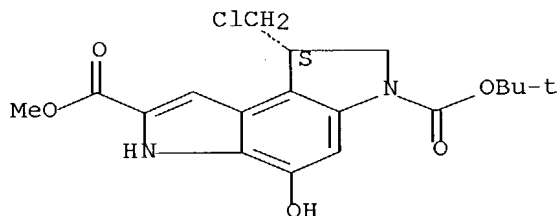
(Reactant or reagent)

(preparation of intermediates for preparation of duocarmycin SA and its derivs.)

RN 144786-07-2 CAPLUS

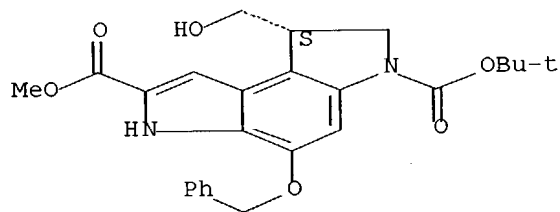
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



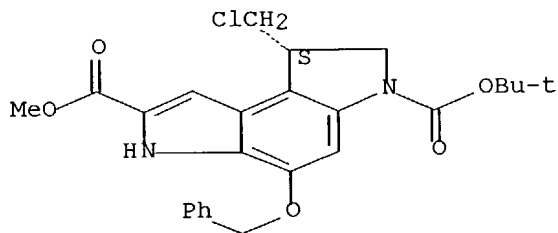
RN 197657-12-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 197657-13-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



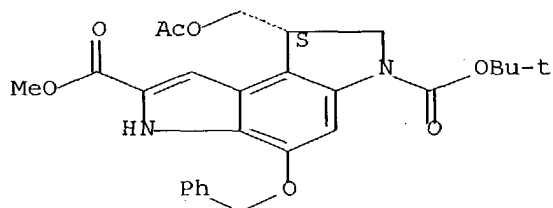
IT 197657-11-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of intermediates for preparation of duocarmycin SA and
its derivs.)

RN 197657-11-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-
dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

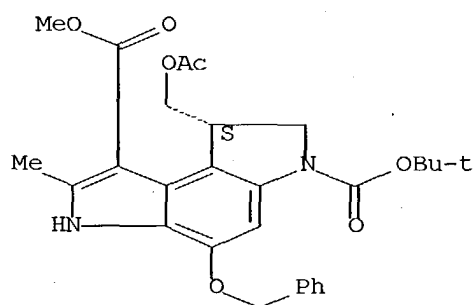
Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

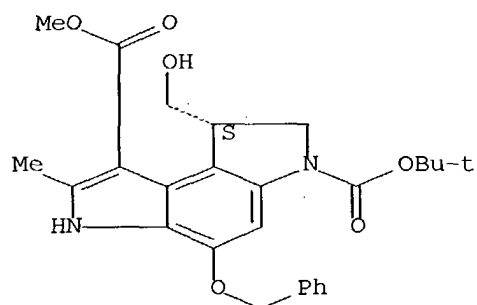
L10 ANSWER 45 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:191565 CAPLUS Full-text
 DN 128:270457
 TI Novel synthesis of optically active CC-1065, U-73,975 (adozelesin),
 U-80,244 (carzelesin), U-77,779 (bizelesin), KW-2189, and DU-86
 AU Fukuda, Yasumichi; Furuta, Hirosuke; Shiga, Futoshi; Asahina, Yoshikazu;
 Terashima, Shiro
 CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Tochigi,
 329-01, Japan
 SO Heterocycles (1997), 45(12), 2303-2308
 CODEN: HTCYAM; ISSN: 0385-5414
 PB Japan Institute of Heterocyclic Chemistry
 DT Journal
 LA English
 OS CASREACT 128:270457
 AB The title syntheses were achieved by the method featuring oxidative
 cyclization of the enamino esters [(S)-13 and (S)-24] derived from the
 5-aminoindoline [(S)-12], acylation with various structural types of
 indole-2-carboxylic acids, and formation of cyclopropapyrroloindole
 moieties.
 IT **156295-31-7P 156295-32-8P 156295-33-9P**
176685-39-5P 205652-13-7P 205652-14-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT
 (Reactant or reagent)
 (synthesis of CC-1065, U-73,975 (adozelesin), U-80,244 (carzelesin),
 U-77,779 (bizelesin), KW-2189, and DU-86)
 RN 156295-31-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



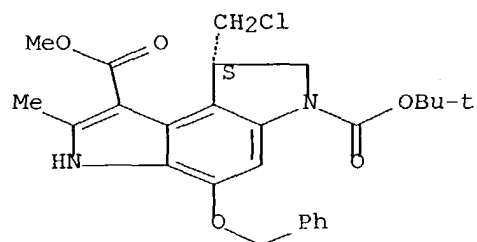
RN 156295-32-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-,
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



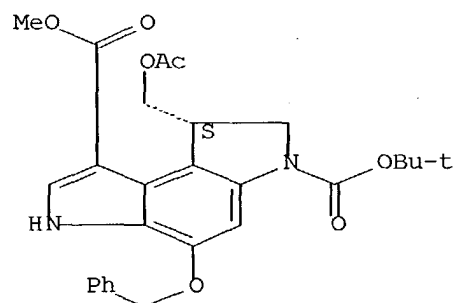
RN 156295-33-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 176685-39-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-
 dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

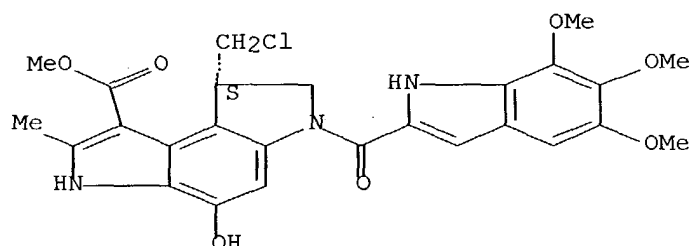
Absolute stereochemistry. Rotation (-).



RN 205652-13-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

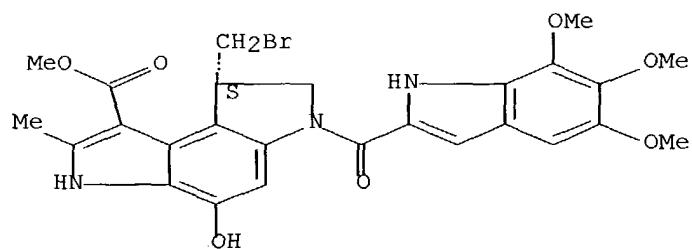
Absolute stereochemistry.



RN 205652-14-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154889-68-6P, KW-2189

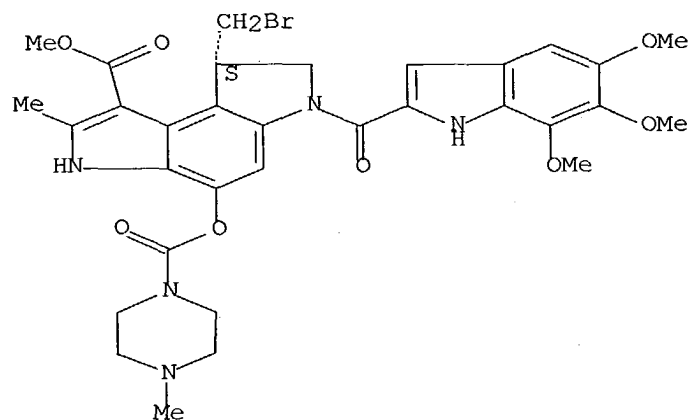
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of CC-1065, U-73,975 (adozelesin), U-80,244 (carzelesin), U-77,779 (bizelesin), KW-2189, and DU-86)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX
NAME)

Absolute stereochemistry.



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 46 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:180874 CAPLUS Full-text

DN 128:243950

TI Preparation of indolylcarbonylbenzindoles and analogs as antitumor prodrugs

IN Denny, William Alexander; Tercel, Moana; Atwell, Graham John

PA Auckland Division Cancer Society of New Zealand Inc., N. Z.; Denny, William Alexander; Tercel, Moana; Atwell, Graham John

SO PCT Int. Appl., 78 pp.

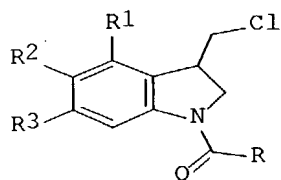
CODEN: PIXXD2

DT Patent

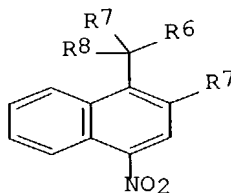
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9811101	A2	19980319	WO 1997-NZ117	19970912
	WO 9811101	A3	19980423		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9744039	A1	19980402	AU 1997-44039	19970912
	AU 721037	B2	20000622		
	EP 938474	A2	19990901	EP 1997-942316	19970912
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	NZ 334344	A	20000825	NZ 1997-334344	19970912
	JP 2000517292	T2	20001226	JP 1997-537492	19970912
	US 6130237	A	20001010	US 1999-266966	19990312
PRAI	GB 1996-19082	A	19960912		
	GB 1997-7394	A	19970410		
	WO 1997-NZ117	W	19970912		
OS	MARPAT 128:243950				
GI					



I



II

AB Title compds. [I; R = heterocyclyl(ethenyl); R1R2 = CH:CHCH:CH, CH:CR5NH, etc.; R3 = NO2, NH2, NHOH, SH, alkylthio, etc.; R4 = halo, OSO2H, alkylsulfonyloxy, etc.; R5 = CO2H, alkoxycarbonyl, etc.] were prepared for use in, e.g., ADEPT therapy. Thus, naphthylmalonate II (R6 = H, R7 = CON3, R7 = R8 = CO2Me) (preparation given) was cyclized to give II (R6R7 = CONH, R7 = R8 = CO2Me) which was converted in 5 steps to II (R6R7 = CH2NCO2CMe3, R7 = CH2Cl, R8 = H). The latter was deprotected and the product N-acylated by 5,6,7-trimethoxyindole-2-carboxylic acid to give I (R = 5,6,7-trimethoxyindol-2-yl, R1R2 = CH:CHCH:CH, R3 = NO2, R4 = Cl). Data for biol. activity of I were given.

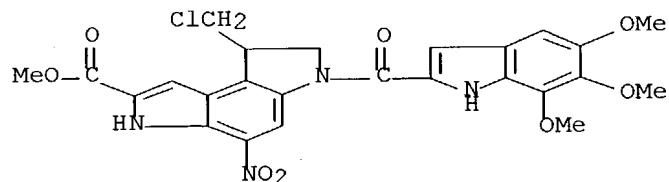
IT 204915-56-0P 204915-58-2P 204915-59-3P
204915-60-6P 204915-61-7P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolylcarbonylbenzindoles and analogs as antitumor
prodrugs)

RN 204915-56-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-
, methyl ester (9CI) (CA INDEX NAME)



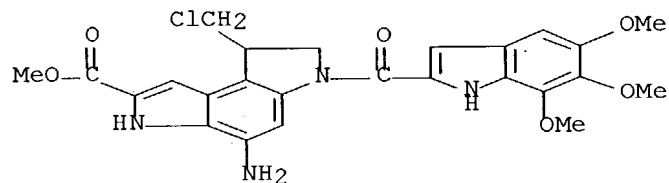
RN 204915-58-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-
(chloromethyl)-
,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl
ester, compd. with ethyl acetate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 204915-57-1

CMF C25 H25 Cl N4 O6



CM 2

CRN 141-78-6

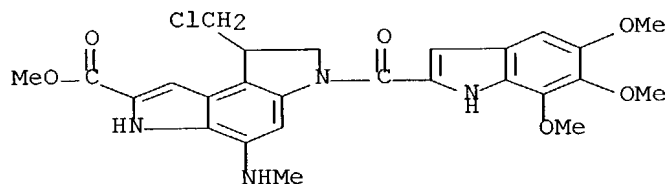
CMF C4 H8 O2

Et-O-Ac

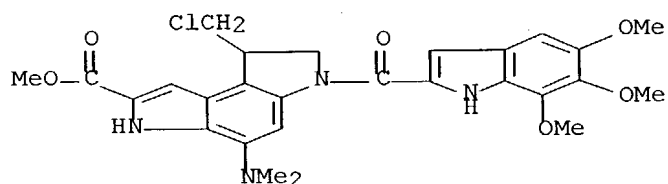
RN 204915-59-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-

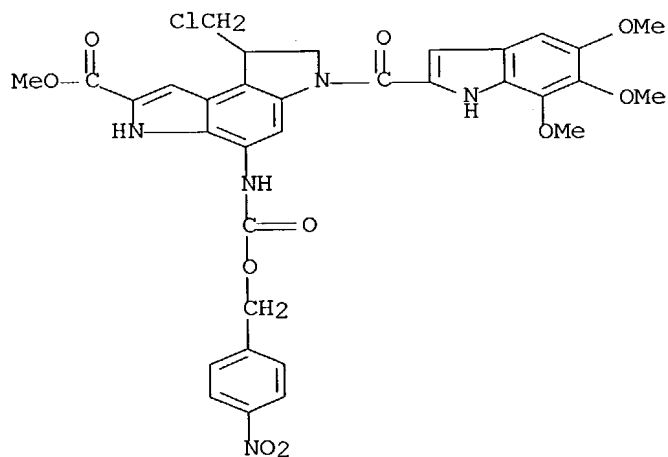
3,6,7,8-
 tetrahydro-4-(methylamino)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-
 methyl ester (9CI) (CA INDEX NAME)



RN 204915-60-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-(dimethylamino)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 204915-61-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-nitrophenyl)methoxy]carbonylamino]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



IT 204916-10-9P 204916-11-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

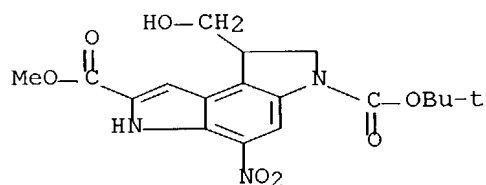
RACT

(Reactant or reagent)

(preparation of indolylcarbonylbenzindoles and analogs as antitumor prodrugs)

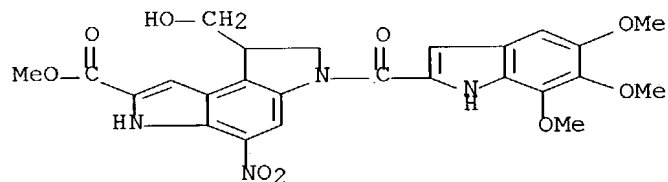
RN 204916-10-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



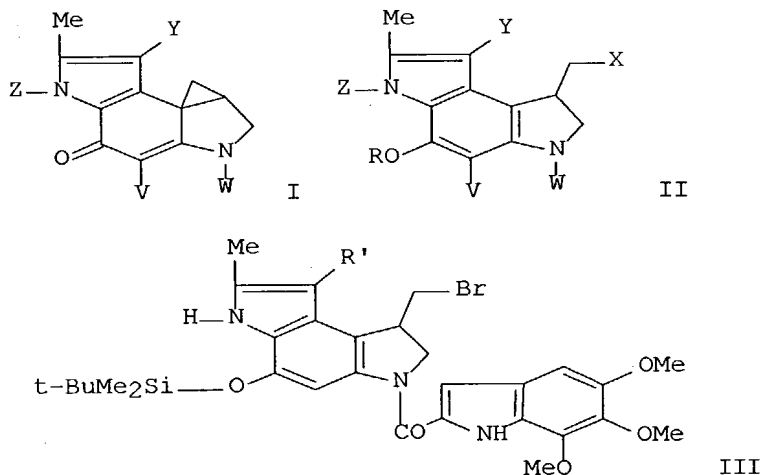
RN 204916-11-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 47 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:175925 CAPLUS Full-text
 DN 128:243875
 TI Preparation of antitumor DC-89 derivatives
 IN Amishiro, Nobuyoshi; Saito, Hiromitsu; Okamoto, Akihiko; Okabe, Masami
 PA Kyowa Hakko Kogyo Co., Ltd., Japan; Amishiro, Nobuyoshi; Saito, Hiromitsu;
 Okamoto, Akihiko; Okabe, Masami
 SO PCT Int. Appl., 100 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9809966	A1	19980312	WO 1997-JP3089	19970903
	W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,				
SE	AU 9741345	A1	19980326	AU 1997-41345	19970903
PRAI	JP 1996-232723		19960903		
	WO 1997-JP3089		19970903		
OS	MARPAT 128:243875				
GI					



AB DC-89 derivs. I and II [Y = H, halo, (un)substituted alkyl, COR1, OR2, SR3, etc.; R1 = H, (un)substituted alkyl, (un)substituted aralkyl, etc.; R2 = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted aryl, etc.; R3 = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted aryl, (un)substituted heterocyclyl; W = H, acyl such as substituted acryloyl, etc.; Z = H, (un)substituted alkyl,

(un)substituted alkenyl, (un)substituted aryl, COR9 , etc.; R9 = H, acyl, silyl; V = H, halo, NO2, etc.; X = Cl, Br; R = H, OH, alkoxy, aryl, etc.] and their pharmaceutically acceptable salts are prepared E.g., the title compound III [R' = Me] was prepared in 56% yield by reduction of III [R' = COOMe] with DIBAL-H in THF. In an in vitro study, II [Y = CH2NMe2, R = V = Z = H, X = Cl, W = 5,6,7-trimethoxy-1H-indol-2-ylcarbonyl] HCl (also prepared) had an IC50 of 0.28 nM against HeLaS3 tumor cells.

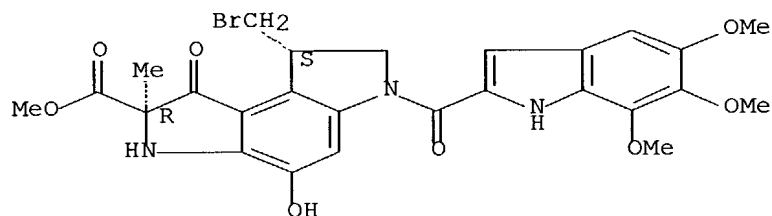
IT **124325-94-6**, DC 89B2

RL: RCT (Reactant); RACT (Reactant or reagent)
(147prepn. of antitumor DC-89 derivs.)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **205050-82-4P 205050-84-6P 205050-96-0P**
205051-09-8P 205051-11-2P 205051-23-6P
205051-29-2P

RL: BAC (Biological activity or effector, except adverse); BSU

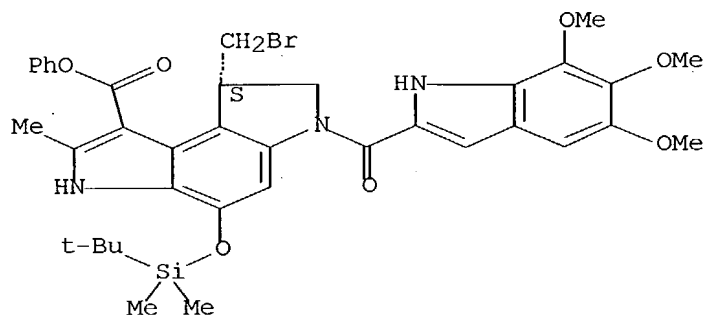
(Biological

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of antitumor DC-89 derivs.)

RN 205050-82-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 205050-84-6 CAPLUS

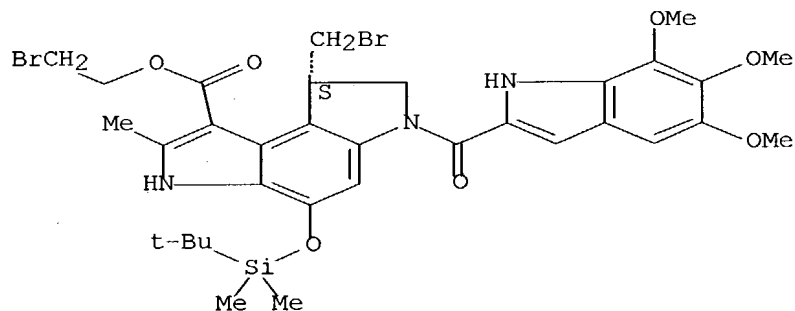
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-bromoethyl ester, (8S)- (9CI)

(CA

INDEX NAME)

Absolute stereochemistry.



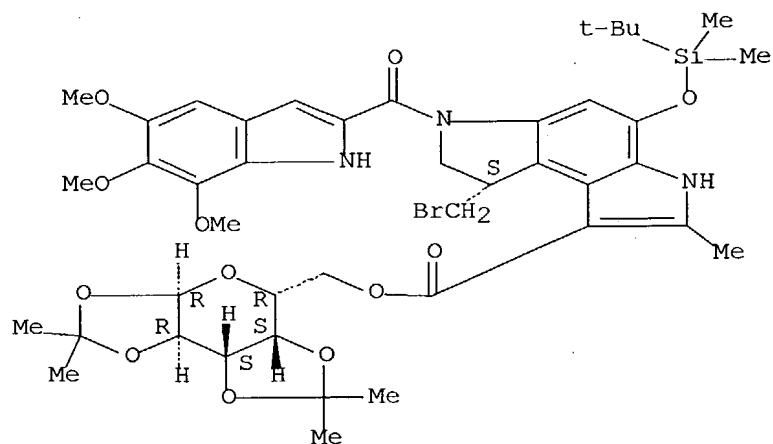
RN 205050-96-0 CAPLUS

CN α -D-Galactopyranose, 1,2:3,4-bis-O-(1-methylethylidene)-,

(8S)-8-(bromomethyl)-4-[[1,1-dimethylethyl]dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-

b:4,3-b']dipyrrole-1-carboxylate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

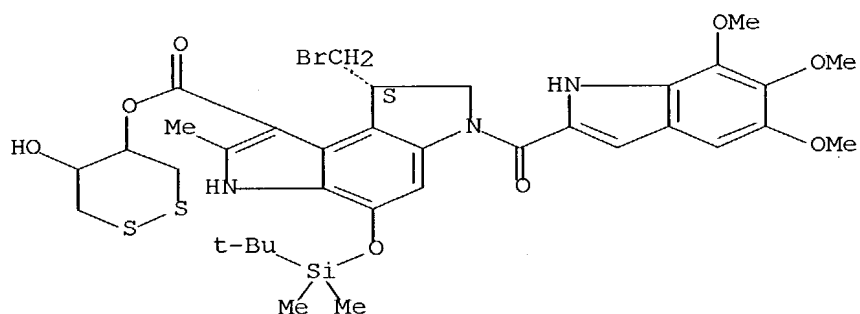


RN 205051-09-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 5-hydroxy-1,2-dithian-4-yl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



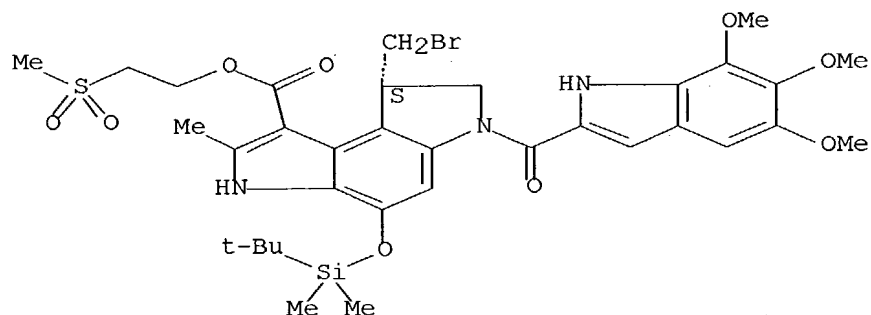
RN 205051-11-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-(methylsulfonyl)ethyl ester, (8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



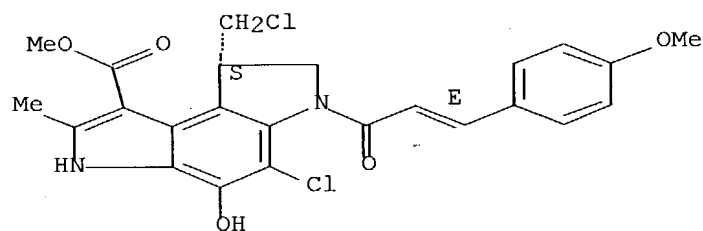
RN 205051-23-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 5-chloro-8-(chloromethyl)-

3,6,7,8-tetrahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



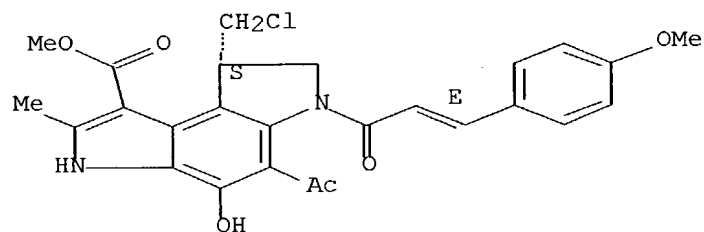
RN 205051-29-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 5-acetyl-8-(chloromethyl)-

3,6,7,8-tetrahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 205050-98-2P 205050-99-3P 205051-00-9P
205051-26-9P 205051-32-7P 205051-34-9P
205051-45-2P 205051-48-5P

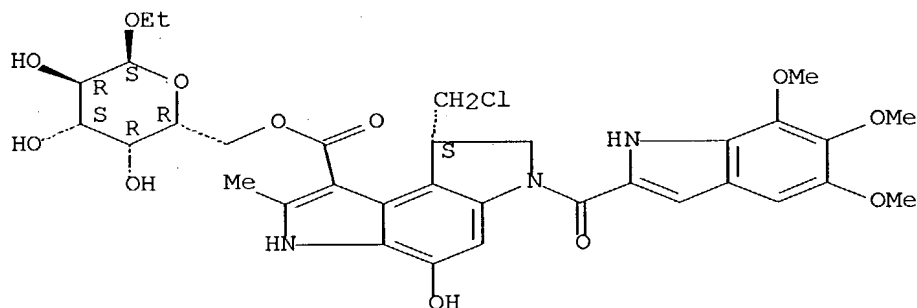
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor DC-89 derivs.)

RN 205050-98-2 CAPLUS

CN α -D-Galactopyranoside, ethyl, 6-[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-1-carboxylate] (9CI) (CA INDEX NAME)

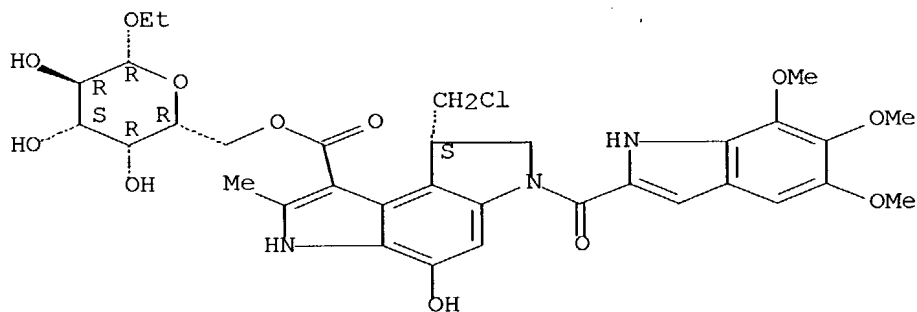
Absolute stereochemistry.



RN 205050-99-3 CAPLUS

CN β -D-Galactopyranoside, ethyl, 6-[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-1-carboxylate] (9CI) (CA INDEX NAME)

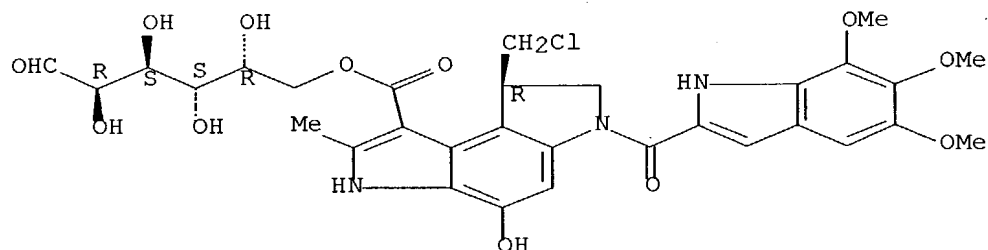
Absolute stereochemistry.



RN 205051-00-9 CAPLUS

CN D-Galactose, 6-[(8R)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-1-carboxylate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 205051-26-9 CAPLUS

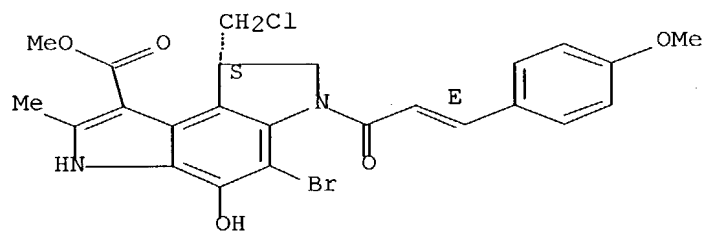
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 5-bromo-8-(chloromethyl)-

3,6,7,8-tetrahydro-4-hydroxy-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-

2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 205051-32-7 CAPLUS

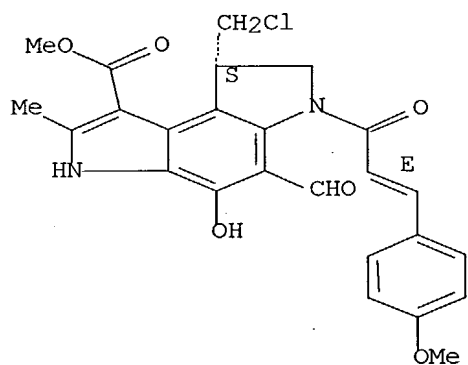
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-5-formyl-

3,6,7,8-tetrahydro-4-hydroxy-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-

2-methyl-, (8S)- (9CI) (CA INDEX NAME)

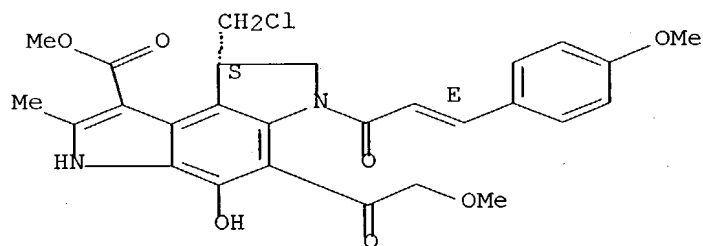
Absolute stereochemistry.

Double bond geometry as shown.



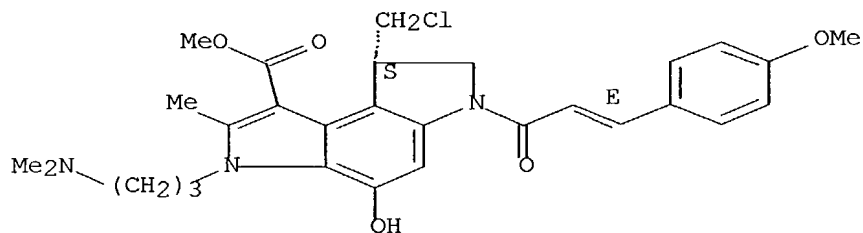
RN 205051-34-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-5-(methoxyacetyl)-6-[(2E)-3-(4-methoxyphenyl)-1-
 oxo-2-
 propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 205051-45-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3-[3-
 (dimethylamino)propyl]-3,6,7,8-tetrahydro-4-hydroxy-6-[3-(4-
 methoxyphenyl)-
 1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrochloride, [S-(E)]-
 (9CI) (CA INDEX NAME)

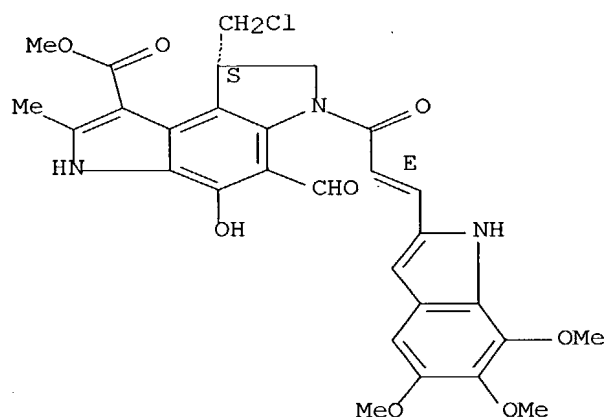
Absolute stereochemistry.
 Double bond geometry as shown.



● HCl

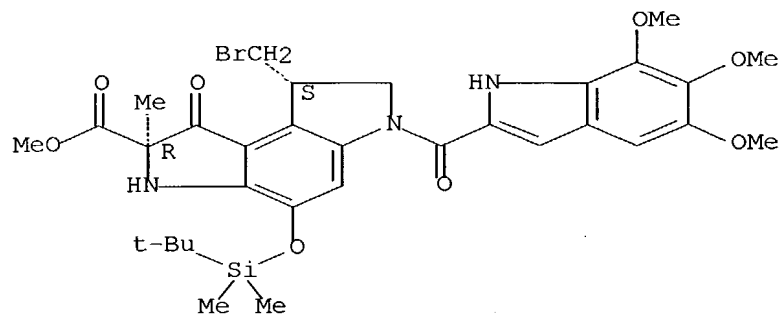
RN 205051-48-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-5-formyl-
 3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(2E)-1-oxo-3-(5,6,7-trimethoxy-1H-indol-2-yl)-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



IT 129953-15-7 177958-19-9 205051-55-4
 205051-56-5 205051-57-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of antitumor DC-89 derivs.)
 RN 129953-15-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[[1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-
 (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 177958-19-9 CAPLUS

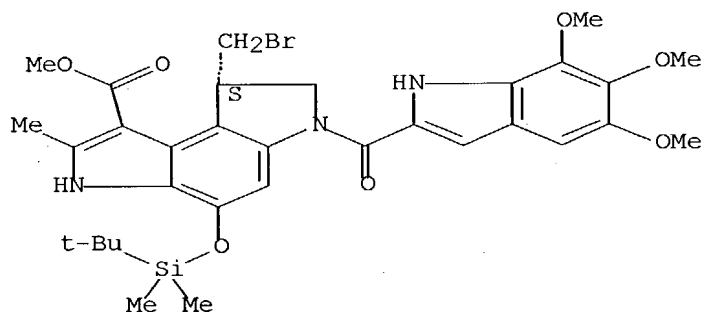
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



RN 205051-55-4 CAPLUS

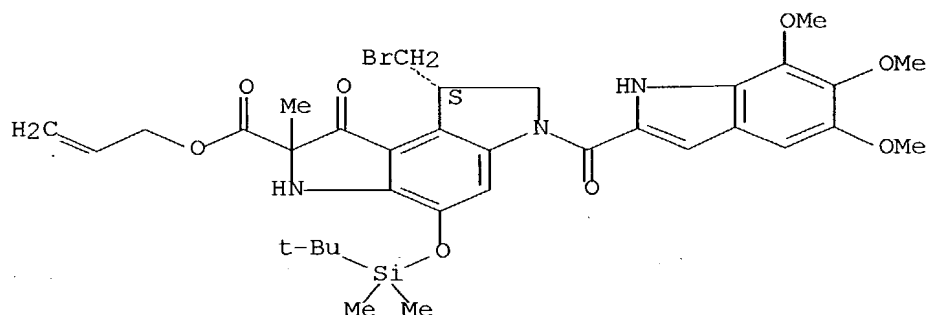
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)-

(9CI)

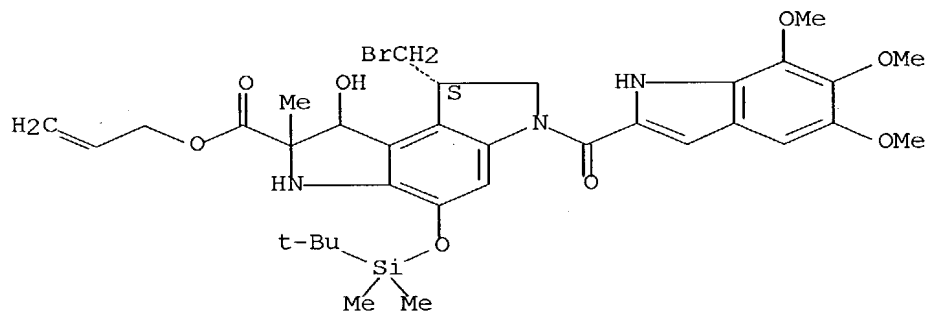
(CA INDEX NAME)

Absolute stereochemistry.



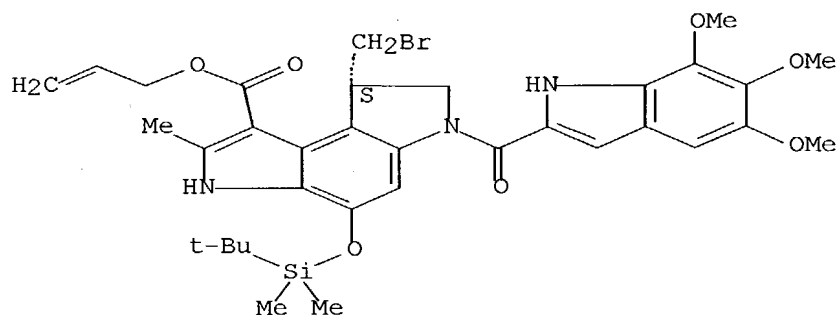
RN 205051-56-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-
 methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester,
 (8S)-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 205051-57-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



IT 205051-58-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

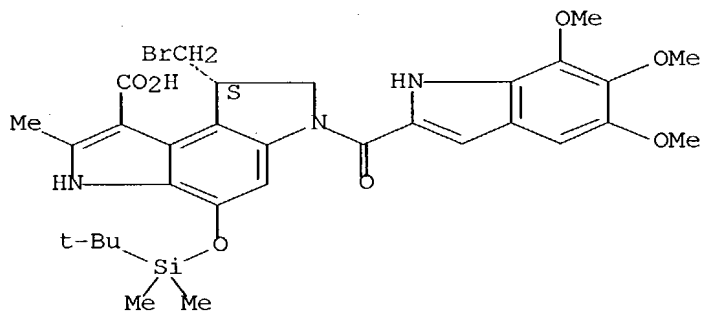
(preparation of antitumor DC-89 derivs.)

RN 205051-58-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

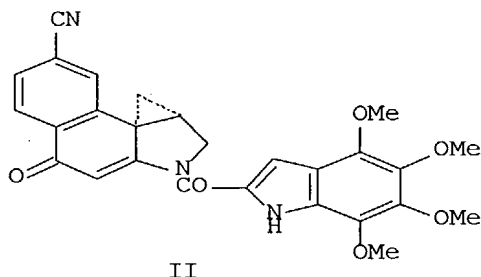
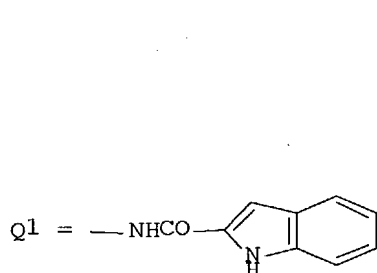
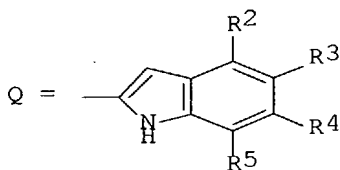
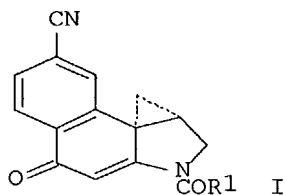


RE.CNT 12

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 48 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:805723 CAPLUS Full-text
 DN 128:61379
 TI Synthesis and cytotoxic activity of analogs of CC-1065 and the
 duocarmycins
 IN Boger, Dale L.
 PA Scripps Research Institute, USA; Boger, Dale L.
 SO PCT Int. Appl., 148 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745411	A1	19971204	WO 1997-US9076	19970530
	W:				
	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
	DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,				
	LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,				
	PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US,				
	UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,				
	GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,				
	ML, MR, NE, SN, TD, TG				
	AU 9732178	A1	19980105	AU 1997-32178	19970530
	EP 934269	A1	19990811	EP 1997-927807	19970530
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO				
	NZ 332960	A	20000526	NZ 1997-332960	19970530
	JP 2000511191	T2	20000829	JP 1997-542909	19970530
	US 6060608	A	20000509	US 1999-194467	19990907
PRAI	US 1996-18860P	P	19960531		
	US 1996-23346P	P	19960912		
	WO 1997-US9076	W	19970530		
OS	MARPAT 128:61379				
GI					



AB Analogs of antitumor antibiotics CC-1065 and the duocarmycins I (R1 = C1-C6-alkyl, Q; R2R3 form a pyrrolidine ring containing the vinylene group with the proviso that R4 and R5 = H; R2 = H and R3 = Q1 with the proviso that R4 and R5 = H; R2 = H, R3, R4, R5 = H, MeO) were prepared as compds. which possess systematic and extensive modifications in the DNA binding subunits attached to a 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The analogs have potent cytotoxic activity and are efficacious antitumor compds. Thus, 3-(tert-butyloxycarbonyl)-1-(chloromethyl)-8-cyano-5-hydroxy-1,2-dihydro-3H-benz[e]indole, prepared in a multistep procedure from m-bromobenzaldehyde and di-Et succinate, was acylated with 5,6,7-trimethoxy-2-indolecarboxylic acid followed by intramol. cyclization to give CCBI-TMI (II). The antitumor IC50(L1210) of II was 7 pM.

IT 182957-20-6P 182957-21-7P 182957-22-8P
182957-23-9P 182957-24-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

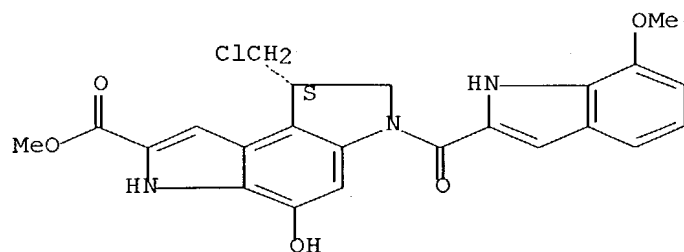
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

RN 182957-20-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(7-methoxy-1H-indol-2-yl)carbonyl]-, methyl
ester,

(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



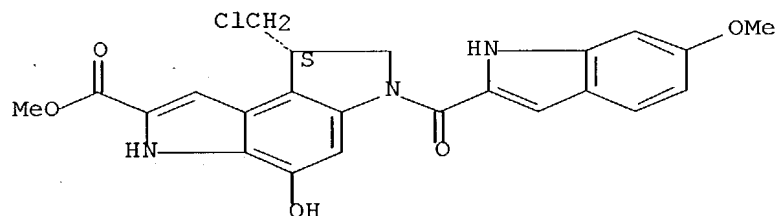
RN 182957-21-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-6-[(6-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,

(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



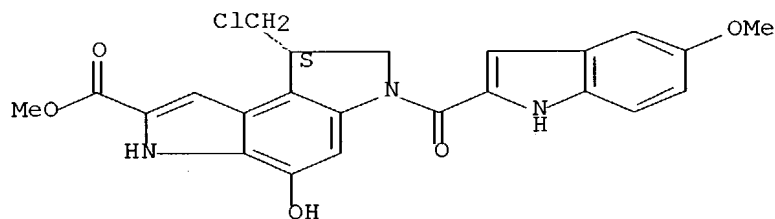
RN 182957-22-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,

(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



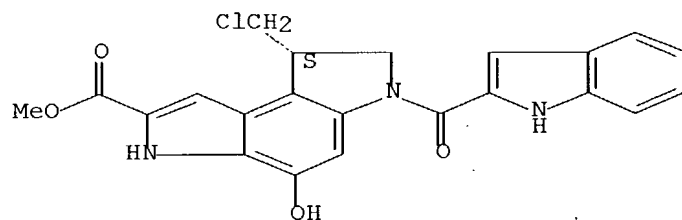
RN 182957-23-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-6-(1H-indol-2-ylcarbonyl)-, methyl ester, (8S)-
(9CI)

(CA INDEX NAME)

Absolute stereochemistry.

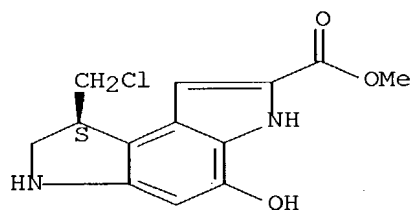


RN 182957-24-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-hydroxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



● HCl

L10 ANSWER 49 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:791611 CAPLUS Full-text

DN 128:110513

TI In vitro enhancement of antitumor activity of a water-soluble
duocarmycin

derivative, KW-2189, by caffeine-mediated DNA-repair inhibition in human
lung cancer cells

AU Ogasawara, Hayato; Nishio, Kazuto; Ishida, Tomoyuki; Arioka, Hitoshi;
Fukuoka, Kazuya; Saijo, Nagahiro

CS Pharmacology Division, National Cancer Center Research Institute, Tokyo,
104, Japan

SO Japanese Journal of Cancer Research (1997), 88(11), 1033-1037

CODEN: JJCREP; ISSN: 0910-5050

PB Japanese Cancer Association

DT Journal

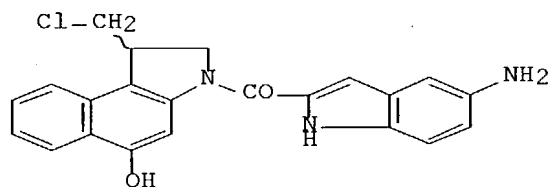
LA English

AB Duocarmycins, including KW-2189, bind in the minor groove of double-
stranded DNA at A-T-rich sequences, followed by covalent bonding with N-
3 of adenine in preferred sequences. We examined the effect of DNA-
repair modulators, such as caffeine and aphidicolin, on the cytotoxicity
of duocarmycins towards human lung cancer cells, as determined by dye
formation assay. Caffeine (0.5 or 1 mM), but not aphidicolin, enhanced
the growth-inhibitory activity of KW-2189, DU-86, and duocarmycin SA.
Caffeine inhibited repair of DNA strand breaks induced by KW-2189, as
assayed by the alkaline elution technique. This suggests that
duocarmycin-induced DNA strand breaks, which are potentially lethal to
cells, are repaired through a caffeine-sensitive pathway.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 50 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:783786 CAPLUS Full-text
 DN 128:48468
 TI Preparation of DNA-binding glucuronide indoles immuno-conjugates as
 antitumors
 IN Wang, Yuqiang; Wright, Susan C.; Larrick, James W.
 PA Panorama Research, Inc., USA
 SO PCT Int. Appl., 79 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9744000	A2	19971127	WO 1997-US9055	19970522
	WO 9744000	A3	19971231		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5843937	A	19981201	US 1996-652883	19960523
	AU 9732170	A1	19971209	AU 1997-32170	19970522
	EP 918752	A2	19990602	EP 1997-927798	19970522
	R:	AT, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE			
	CN 1219841	A	19990616	CN 1997-194862	19970522
	JP 2000511893	T2	20000912	JP 1997-542898	19970522
PRAI	US 1996-652883	A	19960523		
	WO 1997-US9055	W	19970522		
OS	MARPAT 128:48468				
GI					



I

AB The present invention relates to novel DNA alkylating agents and the prodrugs of these agents which are useful as antitumors and DNA labeling agents. The compds. are hydroxydihydrobenzindole oligopeptides and prodrugs thereof wherein the monomeric constituents are derived from monocyclic, or bicyclic heterocyclic aromatic residues. Thus, indole I was prepared and tested for its antitumor activity with cytotoxicity (IC₅₀ = 0.09 nM).

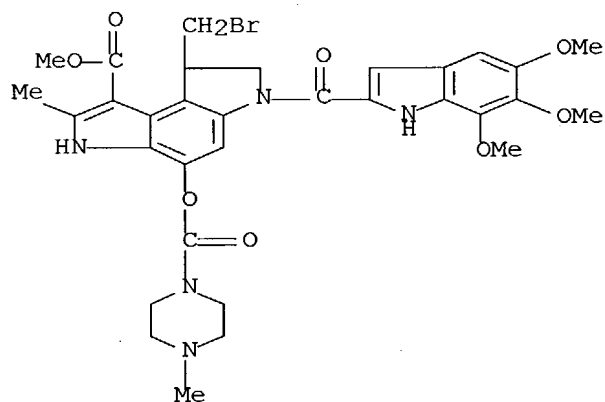
IT 134106-78-8P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);

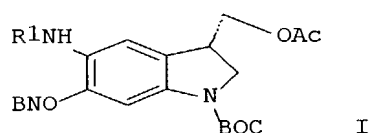
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole
oligopeptides immuno-conjugates as antitumors)

RN 134106-78-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 51 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:707375 CAPLUS Full-text
 DN 127:318803
 TI A novel synthesis of (+)-duocarmycin SA
 AU Fukuda, Yasumichi; Terashima, Shiro
 CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi,
 329-01, Japan
 SO Tetrahedron Letters (1997), 38(41), 7207-7208
 CODEN: TELEAY; ISSN: 0040-4039
 PB Elsevier
 DT Journal
 LA English
 OS CASREACT 127:318803
 GI



AB The title synthesis was achieved in eight steps from (S)-5-aminoindoline
 (I) (R1 = H) by a method featuring sequential dehydrogenation, double
 bond isomerization, and oxidative cyclization of (S)-5-[(1-
 methoxycarbonyl)ethyl]aminoindoline (II) [I, R1 = (S)-CH(Me)CO2Me] as
 the key steps. The sequential reaction was effected by using MnO2-
 Pd(OAc)2 as the oxidizing agent in the presence of an acid catalyst.

IT 144786-07-2P 152785-82-5P 182957-24-0P
 197657-11-7P 197657-12-8P 197657-13-9P

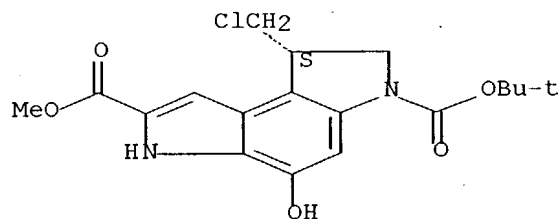
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT
 (Reactant or reagent)
 (synthesis of (+)-duocarmycin SA)

RN 144786-07-2 CAPLUS

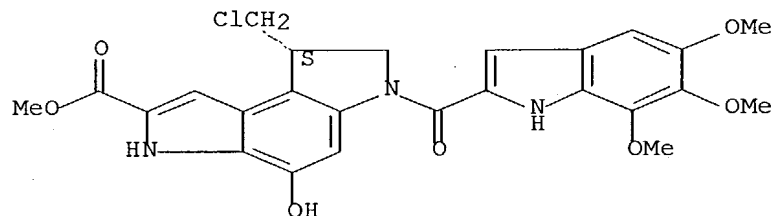
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
 ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



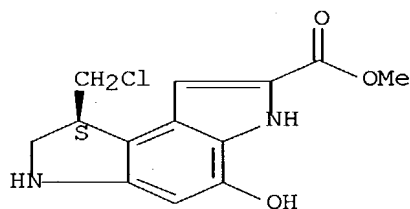
RN 152785-82-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl
 ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182957-24-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
 INDEX NAME)

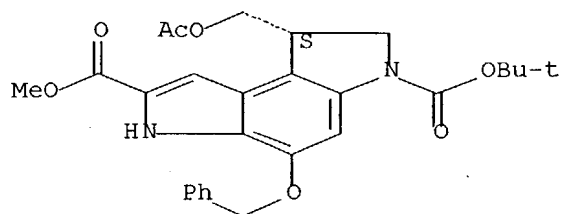
Absolute stereochemistry.



● HCl

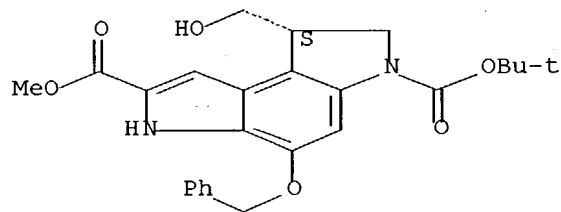
RN 197657-11-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-
 dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



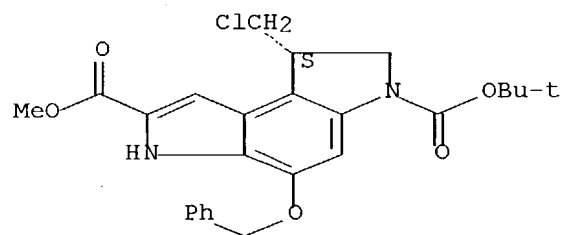
RN 197657-12-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 197657-13-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 52 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:468982 CAPLUS Full-text

DN 127:185373

TI Synthesis and antitumor activity of novel cyclopropapyrroloindole (CPI) derivatives bearing methoxycarbonyl and trifluoromethyl groups

AU Fukuda, Yasumichi; Furuta, Hirosuke; Shiga, Futoshi; Oomori, Yasuo; Kusama, Yoshie; Ebisu, Hiroyuki; Terashima, Shiro

CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi, 329-01, Japan

SO Bioorganic & Medicinal Chemistry Letters (1997), 7(13), 1683-1688
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

DT Journal

LA English

AB The title synthesis was achieved by employing oxidative cyclization of the enamino ester as a key step. Some of these novel 3-methoxycarbonyl-2-trifluoromethylcyclopropapyrroloindole (MCTFCPI) derivs. were found to exhibit antitumor activity against murine leukemia and murine solid tumors more prominent than that of known CPI derivs.

IT **194361-61-0P**

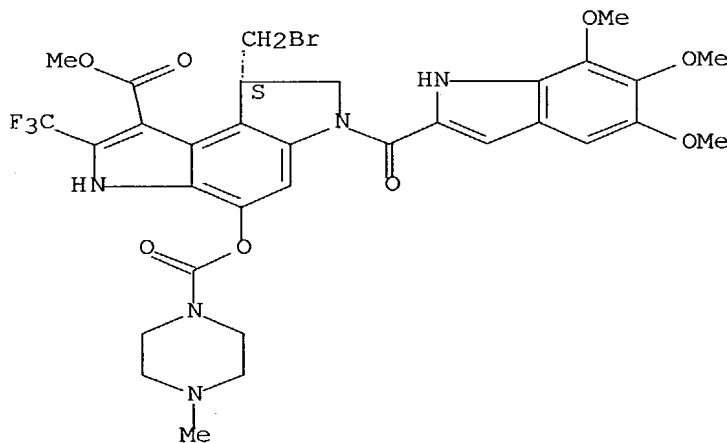
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (synthesis and antitumor activity of cyclopropapyrroloindole derivs. bearing methoxycarbonyl and trifluoromethyl groups)

RN 194361-61-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 2-A

● HCl

IT **154889-68-6**, KW 2189

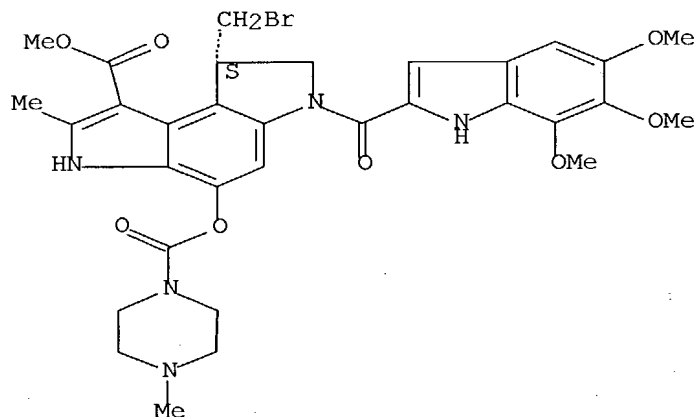
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (synthesis and antitumor activity of cyclopropapyrroloindole derivs.)

bearing methoxycarbonyl and trifluoromethyl groups)

RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

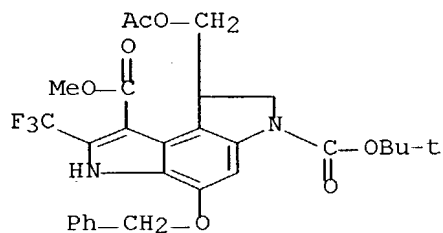


IT 194093-62-4P 194093-63-5P 194093-64-6P
194093-65-7P 194093-66-8P 194093-68-0P
194093-69-1P 194093-70-4P 194093-71-5P
194361-62-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT(Reactant or reagent)(synthesis and antitumor activity of
cyclopropapyrroloindole derivs. bearing methoxycarbonyl and
trifluoromethyl groups)

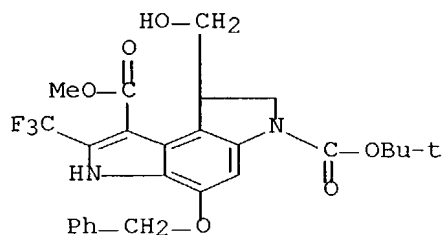
RN 194093-62-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-
, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



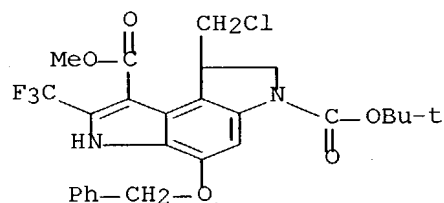
RN 194093-63-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



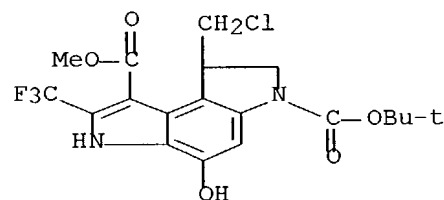
RN 194093-64-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



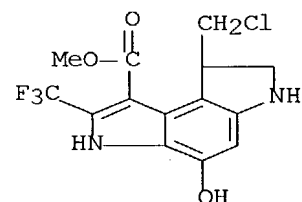
RN 194093-65-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-66-8 CAPLUS

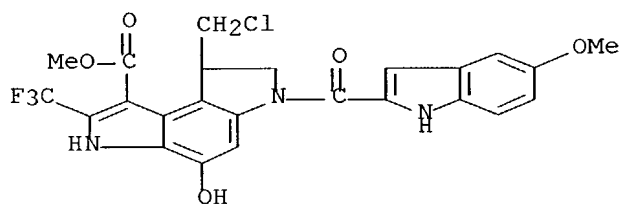
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester,
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

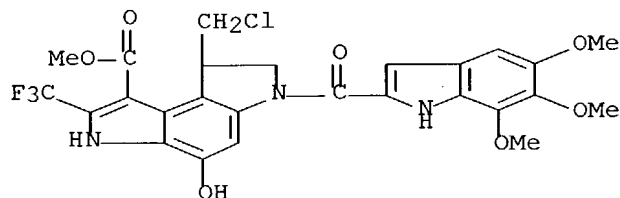
RN 194093-68-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-2-
(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



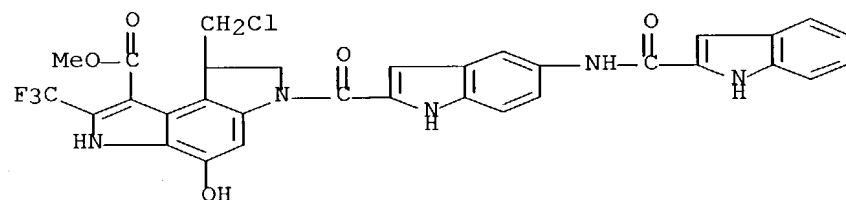
RN 194093-69-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



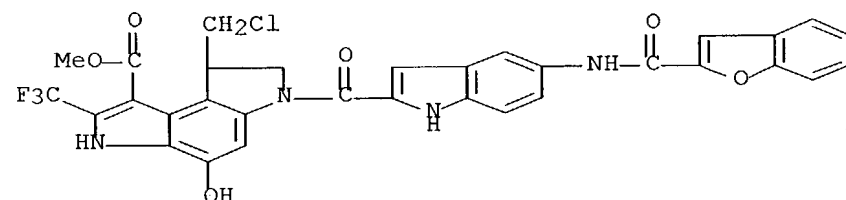
RN 194093-70-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 194093-71-5 CAPLUS

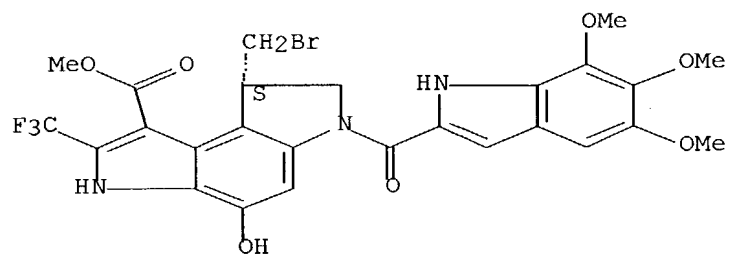
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 194361-62-1 CAPLUS

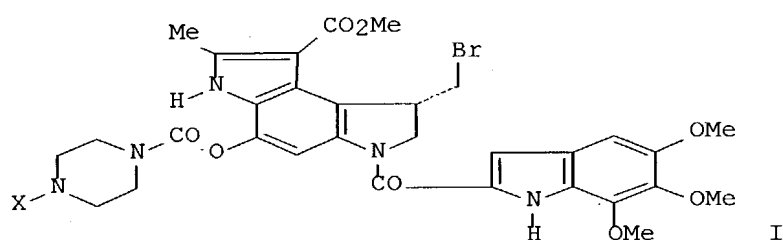
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 53 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:404887 CAPLUS Full-text
 DN 127:108790
 TI The synthesis of [3H]KW-2189, a novel active antitumor antibiotic
 AU Nagamura, Satoru; Kinugawa, Masahiko; Ogasa, Takehire; Saito, Hiromitsu
 CS Kyowa Hakko Kogyo Co. Ltd., Tokyo Research Laboratories, Machida, 194,
 Japan
 SO Journal of Labelled Compounds & Radiopharmaceuticals (1997), 39(6),
 471-477
 CODEN: JLCRD4; ISSN: 0362-4803
 PB Wiley
 DT Journal
 LA English
 GI



AB The synthesis of [3H]KW-2189 (I, X = C3H3), a novel active antitumor antibiotic, is described. The key intermediate I (X = H) in the synthesis, was synthesized in four steps from duocarmycin B2. Treatment of I (X = H) with [3H]methyl iodide in the presence of NaHCO₃ in MeOH-Me₂CO (1:1) afforded the [3H]KW-2189 with highly specific activity of 86.4 Ci/mmol.

IT 192509-06-1P

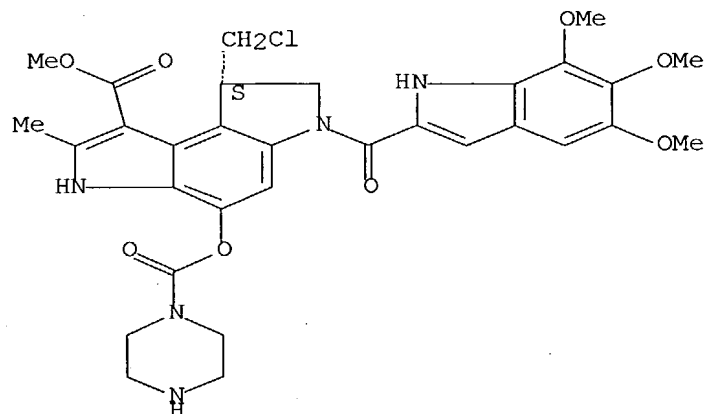
RL: BYP (Byproduct); PREP (Preparation)
 (preparation of [3H]KW-2189)

RN 192509-06-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-

1H- tetrahydro-2-methyl-4-[(1-piperazinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-
 indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



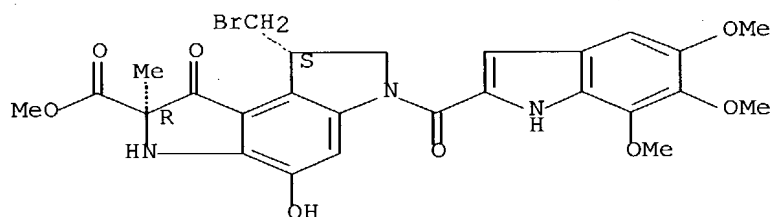
IT 124325-94-6, Duocarmycin B2

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of [3H]KW-2189)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 192509-07-2P 192509-08-3P 192509-09-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

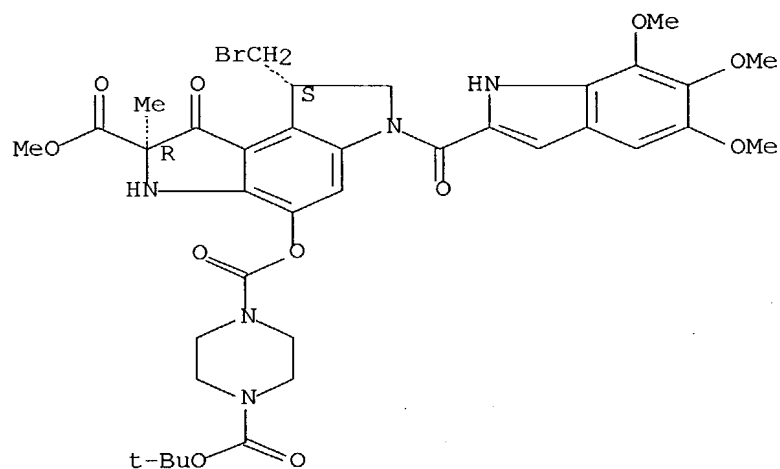
RACT

(Reactant or reagent)
(preparation of [3H]KW-2189)

RN 192509-07-2 CAPLUS

CN 1,4-Piperazinedicarboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-
2-
(methoxycarbonyl)-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-
yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl 1,1-dimethylethyl ester,
(2R-trans)- (9CI) (CA INDEX NAME)

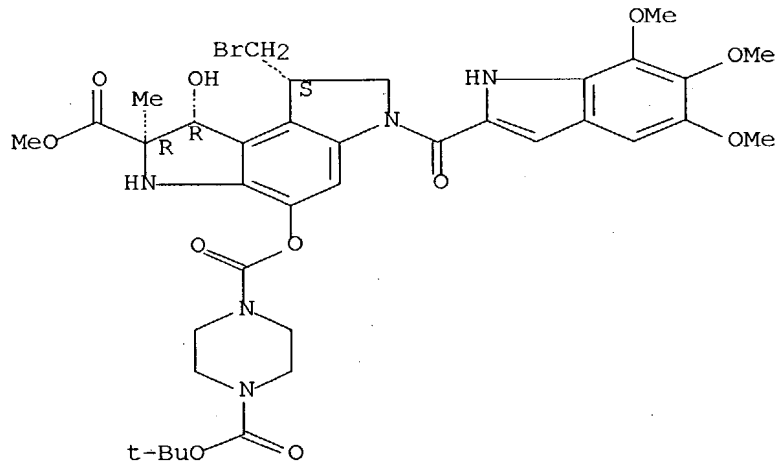
Absolute stereochemistry.



RN 192509-08-3 CAPLUS

CN 1,4-Piperazinedicarboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-(methoxycarbonyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl 1,1-dimethylethyl ester, [1R-(1 α ,2 β ,8 α)]- (9CI) (CA INDEX NAME)

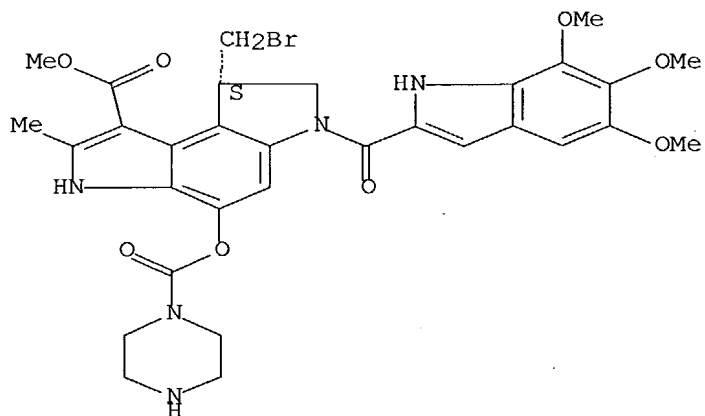
Absolute stereochemistry.



RN 192509-09-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-piperazinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 192509-10-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of [3H]KW-2189)

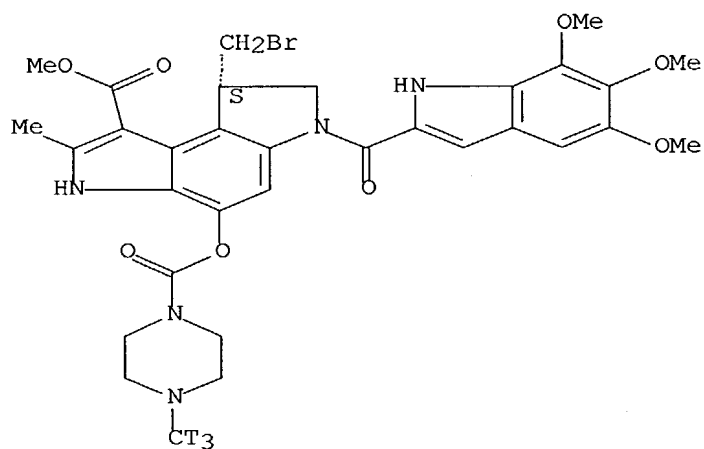
RN 192509-10-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-(methyl-t3)-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI)

(CA

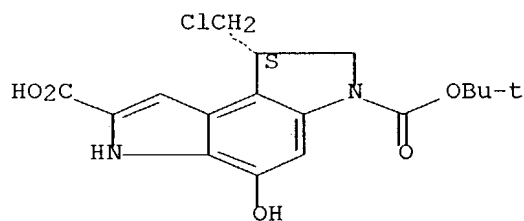
INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 54 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:324292 CAPLUS Full-text
 DN 127:249
 TI Reversed and Sandwiched Analogs of Duocarmycin SA: Establishment of the Origin of the Sequence-Selective Alkylation of DNA and New Insights into the Source of Catalysis
 AU Boger, Dale L.; Bollinger, Bernd; Hertzog, Donald L.; Johnson, Douglas S.;
 Cai, Hui; Mesini, Philippe; Garbaccio, Robert M.; Jin, Qing; Kitos, Paul A.
 CS Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037, USA
 SO Journal of the American Chemical Society (1997), 119(21), 4987-4998
 CODEN: JACSAT; ISSN: 0002-7863
 PB American Chemical Society
 DT Journal
 LA English
 AB The synthesis and examination of two unique classes of duocarmycin SA analogs are described which we refer to as reversed and sandwiched analogs. Their examination was found to establish both the origin of the DNA alkylation selectivity and that both enantiomers of this class of natural products are subject to the same polynucleotide recognition features. The most beautiful demonstration of this is the complete switch in the enantiomeric alkylation selectivity of the reversed analogs which is only consistent with the noncovalent binding model and incompatible with alkylation site models of the origin of the DNA alkylation selectivity. In addition, dramatic alterations in the rates of DNA alkylation were observed among the agents and correlate with the presence or absence of an extended, rigid N2 amide substituent. This has led to the proposal of a previously unrecognized source of catalysis for the DNA alkylation reaction which was introduced in the preceding paper of this issue (J. Am. Chemical Society 1997, 119, xxxx).
 IT **190322-73-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (preparation and reaction of, with indoles)
 RN 190322-73-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) ester, (8S)- (9CI) (CA INDEX NAME)

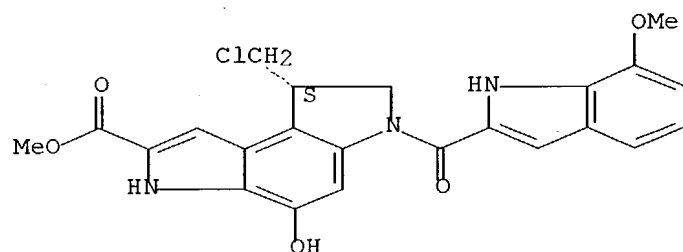
Absolute stereochemistry.



L10 ANSWER 55 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:324291 CAPLUS Full-text
 DN 127:12962
 TI Duocarmycin SA shortened, simplified, and extended agents: a systematic examination of the role of the DNA binding subunit
 AU Boger, Dale L.; Hertzog, Donald L.; Bollinger, Bernd; Johnson, Douglas S.;
 Cai, Hui; Goldberg, Joel; Turnbull, Philip
 CS Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037, USA
 SO Journal of the American Chemical Society (1997), 119(21), 4977-4986
 CODEN: JACSAT; ISSN: 0002-7863
 PB American Chemical Society
 DT Journal
 LA English
 AB The examination of shortened, simplified, and extended analogs of duocarmycin SA are described and constitute a detailed study of the role of linked DNA binding subunit. In addition to enhancing the DNA binding affinity and selectivity through minor groove noncovalent contacts, the studies in conjunction with those of the accompanying article illustrate that an extended rigid N2 amide substituent is required for catalysis of the DNA alkylation reaction. This activation for DNA alkylation is independent of pH, and we propose it results from a binding-induced conformational change in the agents which increases their inherent reactivity. The ground state destabilization of the substrate results from a twist in the linking amide that disrupts the vinylogous amide stabilization of the alkylation subunit and activates the agent for nucleophilic addition. This leads to preferential activation of the agents for DNA alkylation within the narrower, deeper AT-rich minor groove sites where the inherent twist in the linking amide and helical rise of the bound conformation is greatest. Thus, shape-selective recognition (preferential AT-rich noncovalent binding) and shape-dependent catalysis (induced twist in linking N2 amide) combine to restrict SN2 alkylation to accessible adenine N3 nucleophilic sites within the preferred binding sites. Addnl. ramifications of this DNA binding-induced conformational change on the reversibility of the DNA alkylation reaction are discussed. The results of the study illustrate the importance of the C5' methoxy group and the C6 Me ester of duocarmycin SA, and a previously unrecognized role for these substituents is proposed.
 IT 182957-20-6P 182957-21-7P 182957-22-8P
 182957-23-9P 190060-24-3P 190060-25-4P
 190060-26-5P 190060-27-6P 190060-28-7P
 190060-35-6P 190060-36-7P 190060-37-8P
 190060-38-9P 190060-39-0P 190060-40-3P
 190060-42-5P 190060-43-6P 190060-44-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation);
 BIOL (Biological study); PREP (Preparation)
 (duocarmycin SA shortened, simplified, and extended agents: a systematic examination of the role of the DNA binding subunit)
 RN 182957-20-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

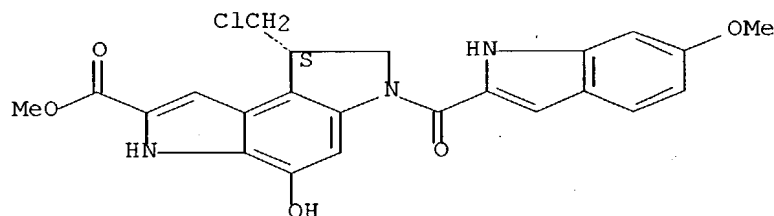
tetrahydro-4-hydroxy-6-[(7-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



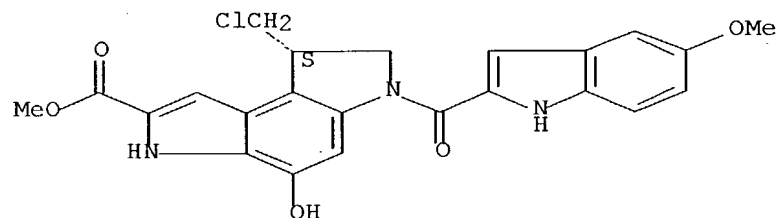
RN 182957-21-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(6-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



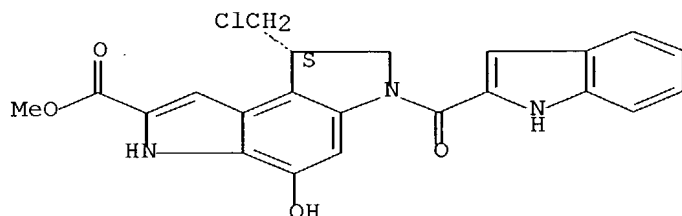
RN 182957-22-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



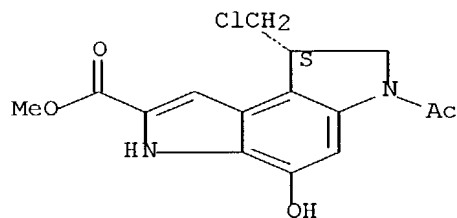
RN 182957-23-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-(1H-indol-2-ylcarbonyl)-, methyl ester, (8S)-
 (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



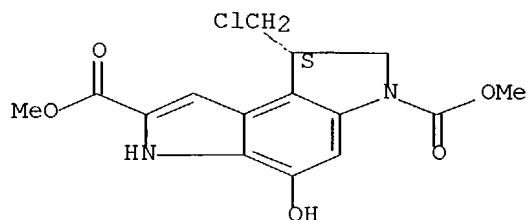
RN 190060-24-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-8-
 (chloromethyl)-
 3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry. Rotation (-).



RN 190060-25-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, dimethyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

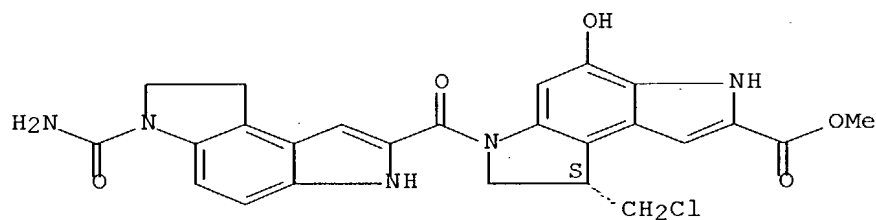
Absolute stereochemistry. Rotation (-).



RN 190060-26-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[6-(aminocarbonyl)-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

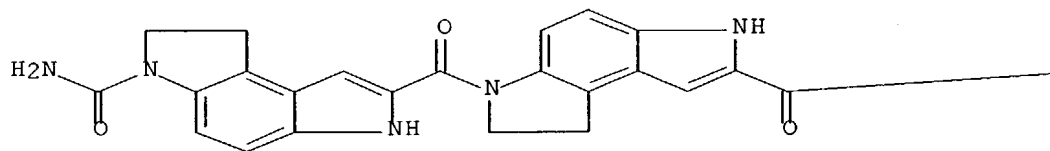
Absolute stereochemistry. Rotation (+).



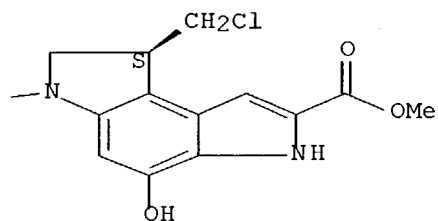
RN 190060-27-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[6-[[6-(aminocarbonyl)-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



PAGE 1-A

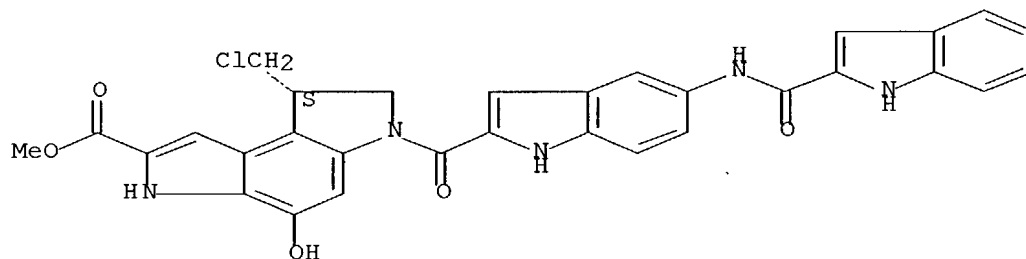


RN 190060-28-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

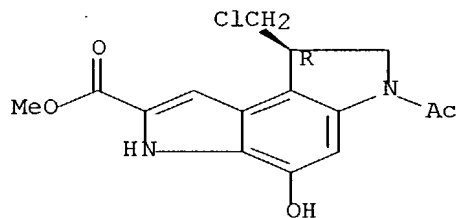
Absolute stereochemistry. Rotation (+).



RN 190060-35-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

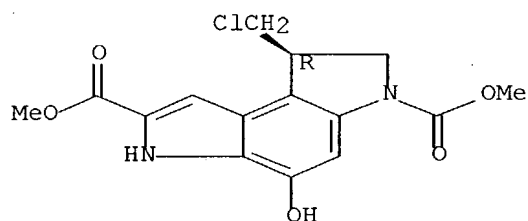


RN 190060-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, dimethyl ester, (8R)-(9CI)

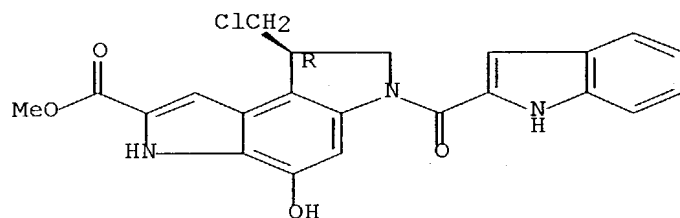
(CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).



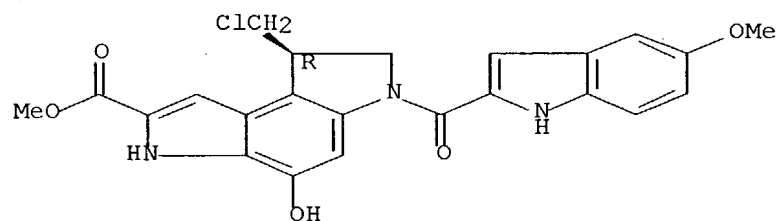
RN 190060-37-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-(1H-indol-2-ylcarbonyl)-, methyl ester, (R)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



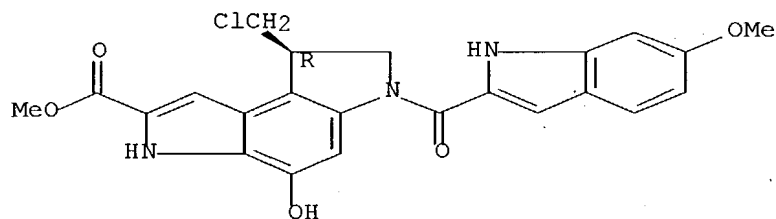
RN 190060-38-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-, methyl
ester,
(8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



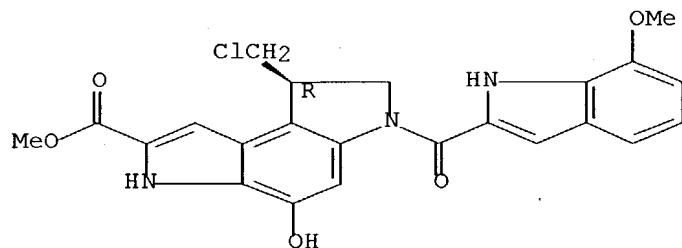
RN 190060-39-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(6-methoxy-1H-indol-2-yl)carbonyl]-, methyl
 ester,
 (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



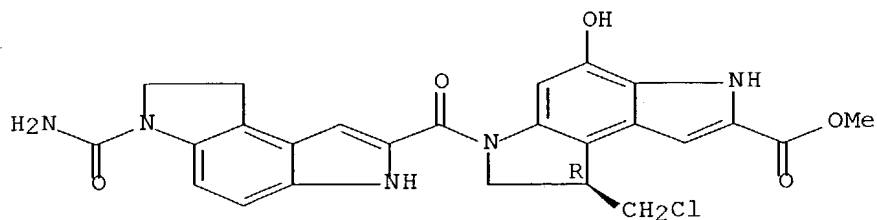
RN 190060-40-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(7-methoxy-1H-indol-2-yl)carbonyl]-, methyl
 ester,
 (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 190060-42-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[6-(aminocarbonyl)-
 3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-
 (chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8R)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

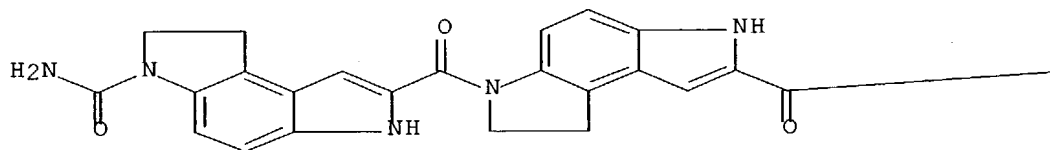


RN 190060-43-6 CAPLUS

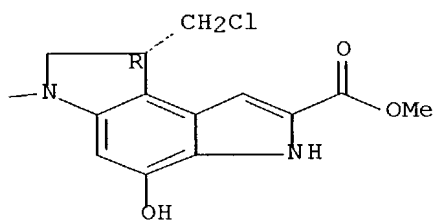
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[[(8R)-6-[[6-(aminocarbonyl)-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydrobenzo[1,2-b:4,3-b']dipyrrol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



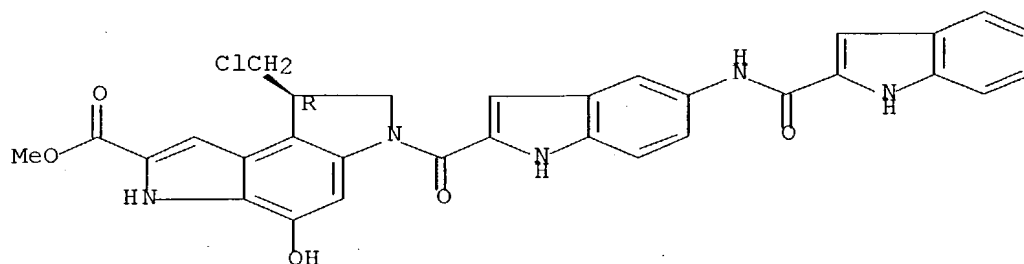
PAGE 1-B



RN 190060-44-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



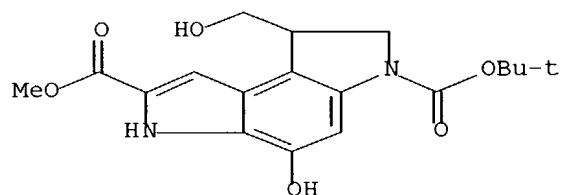
IT **144667-36-7 144667-37-8**

RL: RCT (Reactant); RACT (Reactant or reagent)

(duocarmycin SA shortened, simplified, and extended agents: a systematic examination of the role of the DNA binding subunit)

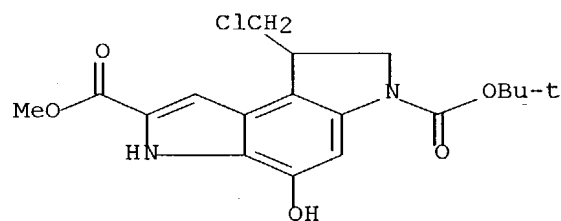
RN 144667-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-4-hydroxy-8-(hydroxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 144667-37-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



IT **181417-69-6P 182957-24-0P 190060-22-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

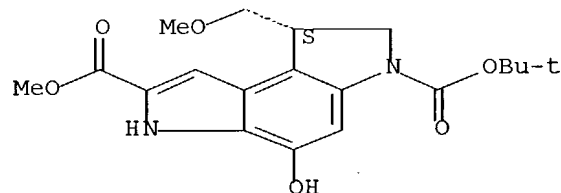
(Reactant or reagent)

(duocarmycin SA shortened, simplified, and extended agents: a systematic examination of the role of the DNA binding subunit)

RN 181417-69-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-4-hydroxy-8-(methoxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl ester, (8S)- (9CI) (CA INDEX NAME)

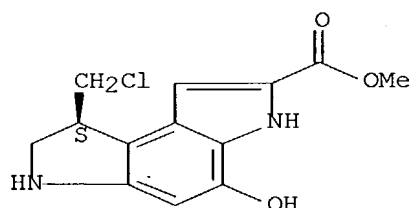
Absolute stereochemistry.



RN 182957-24-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

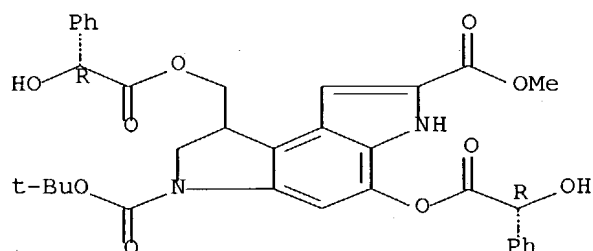


● HCl

RN 190060-22-1 CAPLUS

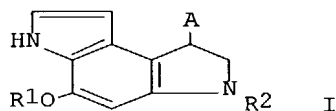
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-4-[(hydroxyphenylacetyl)oxy]-8-[[[(hydroxyphenylacetyl)oxy]methyl]-, 6-(1,1-dimethylethyl) 2-methyl ester, [4(R),8(R)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 56 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:262265 CAPLUS Full-text
 DN 126:277505
 TI Preparation of 8-methylpyrroloindole derivatives as antibiotics and
 antitumor agents
 IN Fukuda, Yasuji; Furuta, Kosuke; Terajima, Atsuro
 PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
 SO Jpn. Kokai Tokkyo Koho, 3 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

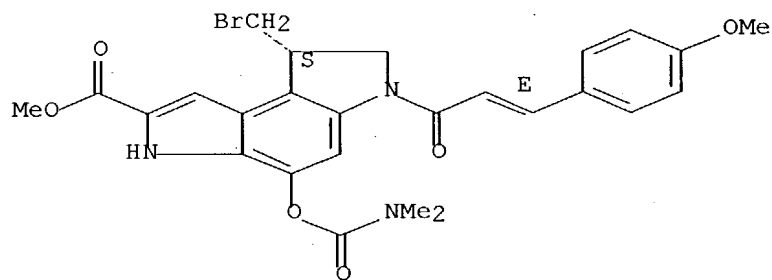
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	JP 09067374	A2	19970311	JP 1995-223056	19950831
PRAI	JP 1995-223056		19950831		
OS	MARPAT 126:277505				
GI					



AB The title compds. [I; Y = Me; R1 = protecting group of amino; A = CH2X1;
 X1 = halo, OH, OSO2R4; R4 = alkyl, aralkyl, (un)substituted aryl, OR5;
 R2, R5 = protecting group of OH] are prepared by reduction of I (Y =
 CO2R3; R3 = linear or branched C1-6 alkyl; A = CH2X2; X2 = halo, OH,
 OSO2R4, etc.; R1, R2 = same as above). I, useful as antibiotics and
 antitumor agents (no data) or intermediates thereof, are prepared
 efficiently and easily. Thus, I (Y = CO2Me, A = CH2OAc, R1 = tert-
 butoxycarbonyl, R2 = C6H4CH2) was refluxed with BH3.THF in THF for 19 h
 and treated with aqueous citric acid to give the title compound I (Y =
 Me, A = CH2OH, R1, R2 = same as above).

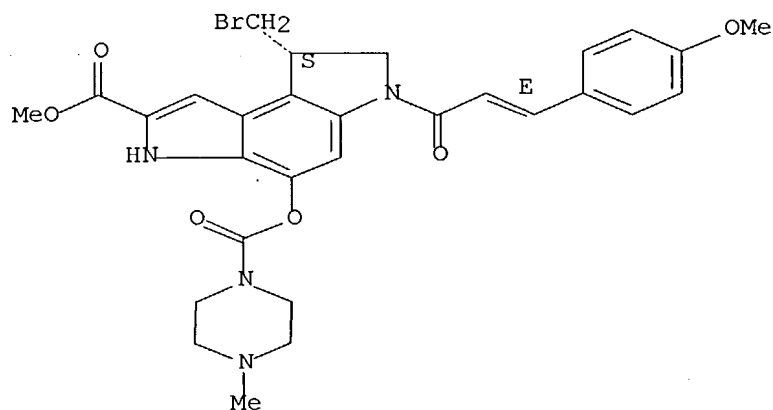
L10 ANSWER 57 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:228843 CAPLUS Full-text
 DN 126:311725
 TI Studies on duocarmycin SA and its derivatives
 AU Nagamura, Satoru; Asai, Akira; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
 CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, Machida, 194, Japan
 SO Bioorganic & Medicinal Chemistry (1997), 5(3), 623-630
 CODEN: BMECEP; ISSN: 0968-0896
 PB Elsevier
 DT Journal
 LA English
 AB New duocarmycin SA derivs. have been synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells, and in vivo antitumor activity against murine sarcoma 180 in mice. The results suggested that the N,N-dialkylcarbamoyl derivs. bearing the p-methoxy cinnamoyl group, prepared from duocarmycin SA, showed good in vivo antitumor activities superior to native duocarmycin SA.
 IT **152718-07-5P 152718-08-6P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (antitumor activity, preparation, and structure of duocarmycin SA derivs.)
 RN 152718-07-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 152718-08-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



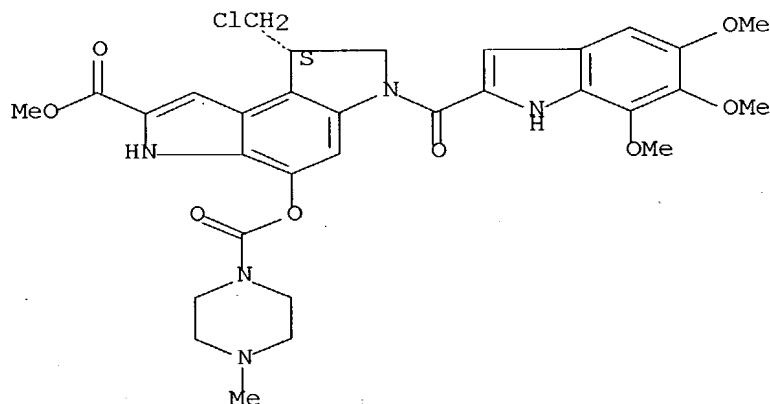
IT 152718-02-0P 152718-03-1P 152718-04-2P
152718-05-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor activity, preparation, and structure of duocarmycin SA derivs.)

RN 152718-02-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

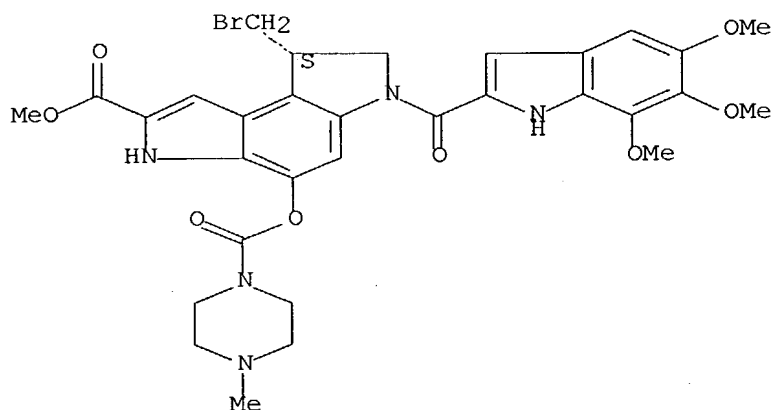
Absolute stereochemistry.



RN 152718-03-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

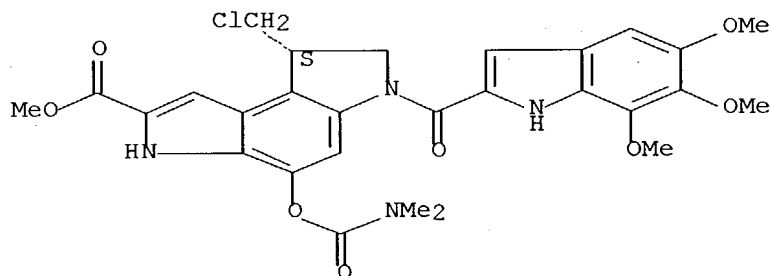
Absolute stereochemistry.



RN 152718-04-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-
 [[(dimethylamino) carbonyl] oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-
 1H-indol-2-yl) carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

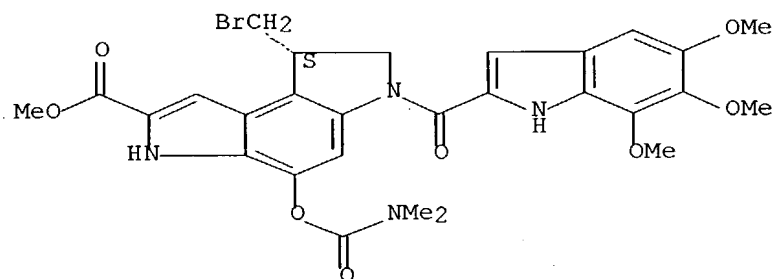
Absolute stereochemistry.



RN 152718-05-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(dimethylamino) carbonyl] oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-
 1H-indol-2-yl) carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 58 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:219845 CAPLUS Full-text

DN 126:287689

TI Synthesis and antitumor activity of novel cyclopropapyrroloindole (CPI) derivatives bearing bis(methoxycarbonyl) groups

AU Fukuda, Yasumichi; Oomori, Yasuo; Kusama, Yoshie; Terashima, Shiro

CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi, 329-01, Japan

SO Bioorganic & Medicinal Chemistry Letters (1997), 7(6), 749-752

CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

DT Journal

LA English

AB The title synthesis was achieved by employing oxidative cyclization of the enaminodiester prepared by Michael addition of the 5-aminoindoline with di-Me acetylenedicarboxylate, as a key step. Some of these novel bis(methoxycarbonyl)cyclopropapyrroloindole (MC2CPI) derivs. 9c, d and their seco-chlorides 18c, d were found to exhibit prominent cytotoxicity and antitumor activity against P388 murine leukemia.

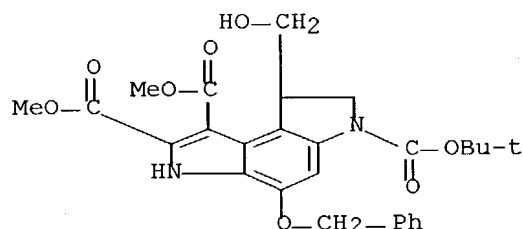
IT **156905-82-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent) (preparation and chlorination of)

RN 156905-82-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



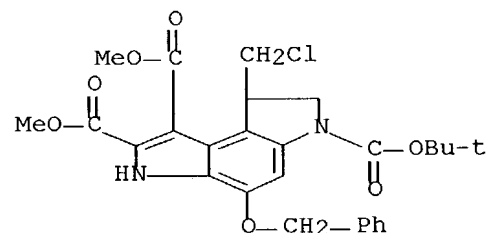
IT **156905-83-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent) (preparation and debenzylation of)

RN 156905-83-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



IT **156905-84-9P**

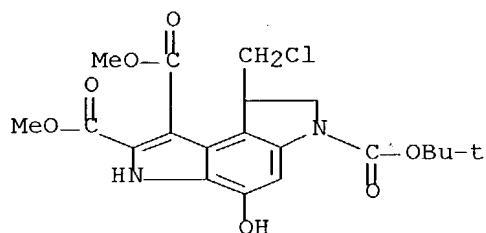
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent) (preparation and deprotection of)

RN 156905-84-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid,

8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl)
1,2-dimethyl ester (9CI) (CA INDEX NAME)

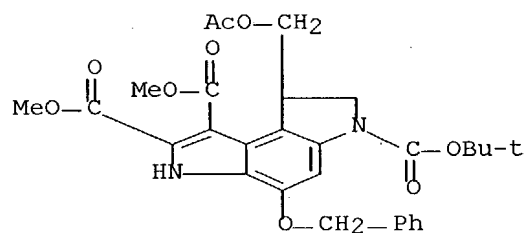


IT 156905-81-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent) (preparation and methanolysis of)

RN 156905-81-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid,
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-
dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



IT 189191-09-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

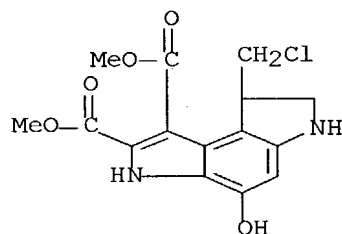
RACT

(Reactant or reagent)

(preparation and reaction of, with indole carboxylates)

RN 189191-09-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-, dimethyl ester, monohydrochloride (9CI)
(CA INDEX NAME)

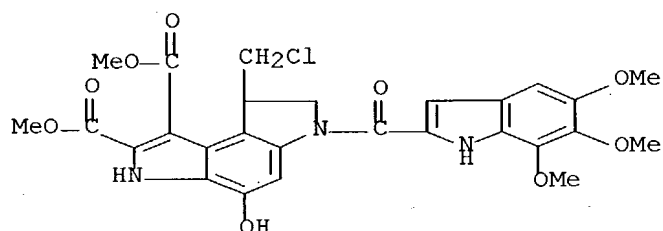


● HCl

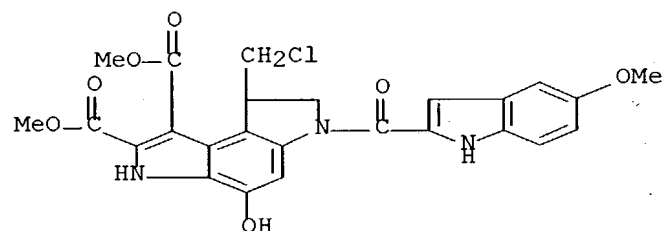
IT 156905-67-8P 156905-68-9P 156905-69-0P

156905-70-3P

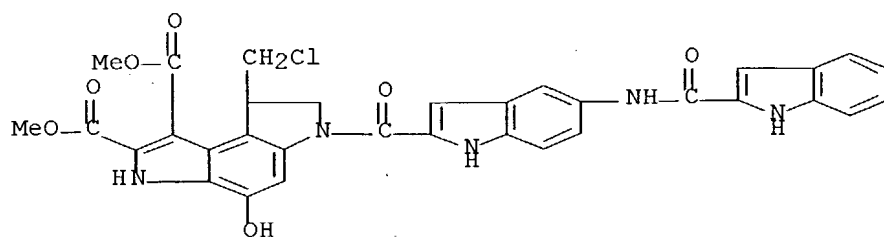
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
(preparation and spirocyclization and antitumor activity of)
RN 156905-67-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-
yl)carbonyl]-
, dimethyl ester (9CI) (CA INDEX NAME)



RN 156905-68-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-,
dimethyl ester (9CI) (CA INDEX NAME)

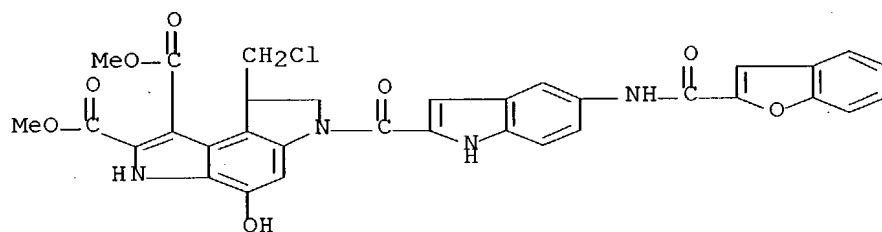


RN 156905-69-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-
indol-
2-yl]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)



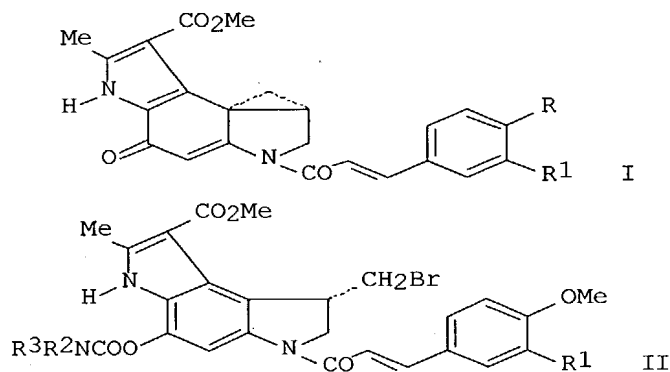
RN 156905-70-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, dimethyl ester (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 59 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:180818 CAPLUS Full-text
 DN 126:157310
 TI Synthesis and Antitumor Activity of Duocarmycin Derivatives: A-Ring
 Pyrrole Compounds Bearing Cinnamoyl Groups
 AU Nagamura, Satoru; Asai, Akira; Amishiro, Nobuyoshi; Kobayashi, Eiji;
 Gomi,
 Katsushige; Saito, Hiromitsu
 CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Machida, 194,
 Japan
 SO Journal of Medicinal Chemistry (1997), 40(6), 972-979
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 GI



AB A series of DU-86 A segment N6-cinnamoyl derivs I (R = OMe, n-propyloxy, allyloxy, pentyloxy, 4-methoxybenzyloxy, OH, NMe₂, NEt₂, Me, Et, NHCO₂CMe₃, NH₂, R₁ = H; R = OMe, R₁ = 3-azidopropyloxy, 3-dimethylaminopropyloxy, OCH₂CO₂CMe₃, OCH₂CO₂Me, NEt₂, NMe₂, NHCO₂CMe₃, NH₂, 3-aminopropyloxy) were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. The 4'-methoxy- and 4'-BocNH-cinnamoyl derivs. exhibited strong in vitro anticellular activity compared to the other synthesized compds. The substitution of the 4'-methoxycinnamoyl derivative did not affect the anticellular activity and contributed to an enhancement of water solubility. Most of the 8-O-carbamoyl derivs. II [R₁ = H, R₃R₂N = 4-methylpyrazinyl, 4-piperidinopiperidinyl, 4-(isopropylaminocarbonylmethyl)piperazinyl; R₁ = NEt₂, NMe₂, 3-aminopropyloxy, NH₂, OCH₂CO₂H, R₃R₂N = 4-methylpyrazinyl] of the 4'-methoxycinnamoyl derivs. displayed remarkably superior in vivo antitumor activity to duocarmycin A or B2. It was noteworthy that these 8-O-carbamoyl derivs. exhibited significant antitumor activity at a wider range of doses as compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in segment B.

IT 186760-19-OP 186760-20-3P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (synthesis and antitumor activity of DU-86, duocarmycin related, derivs. with A-ring pyrrole compds. bearing cinnamoyl groups)

RN 186760-19-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-

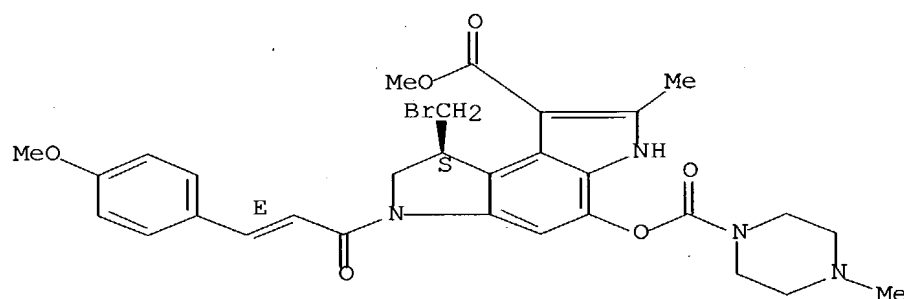
methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.

Double bond geometry as shown.



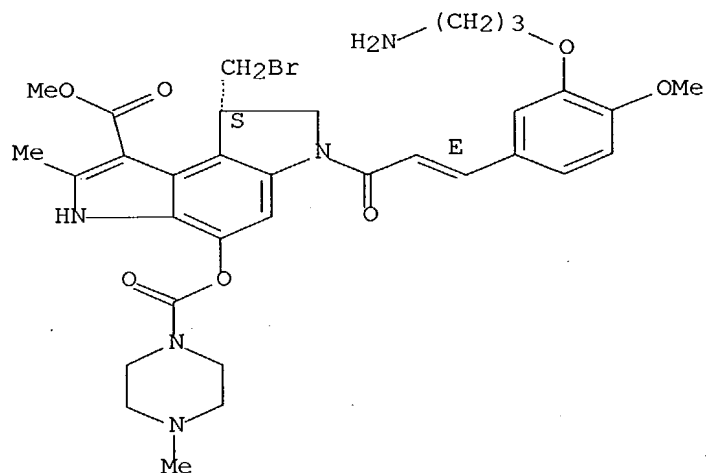
RN 186760-20-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-[3-(3-aminopropoxy)-4-methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, [S-(E)]-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 186760-06-5P 186760-07-6P 186760-08-7P
 186760-09-8P 186760-10-1P 186760-11-2P
 186760-12-3P 186760-21-4P

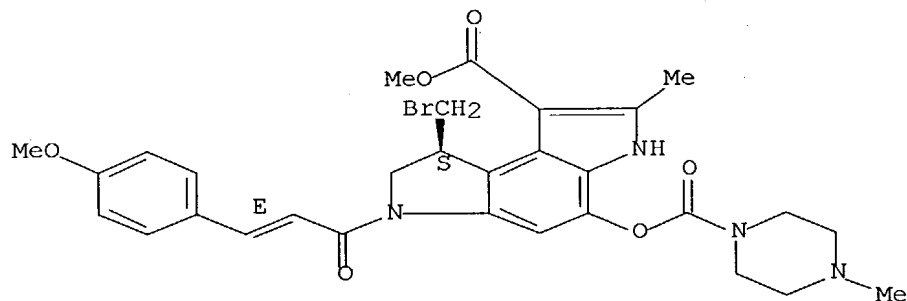
RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation)

(synthesis and antitumor activity of DU-86, duocarmycin related,
 derivs. with A-ring pyrrole compds. bearing cinnamoyl groups)

RN 186760-06-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
 tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-
 [[(4-
 methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride,
 (8S)- (9CI) (CA INDEX NAME)

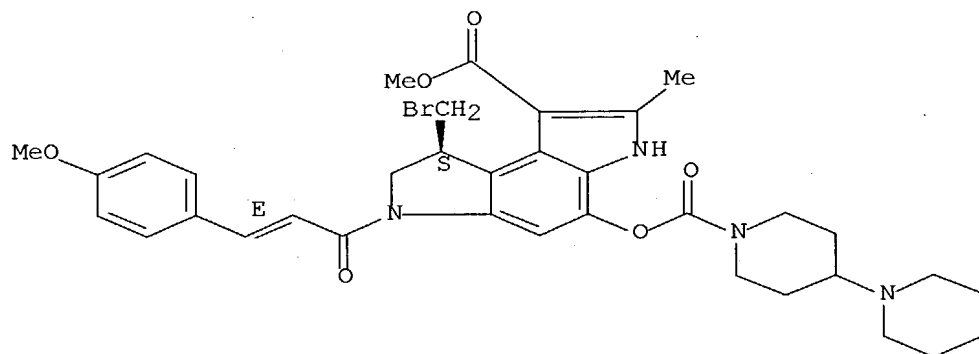
Absolute stereochemistry.
 Double bond geometry as shown.



● HCl

RN 186760-07-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-ylcarbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrochloride, [S-(E)]-(9CI) (CA INDEX NAME)

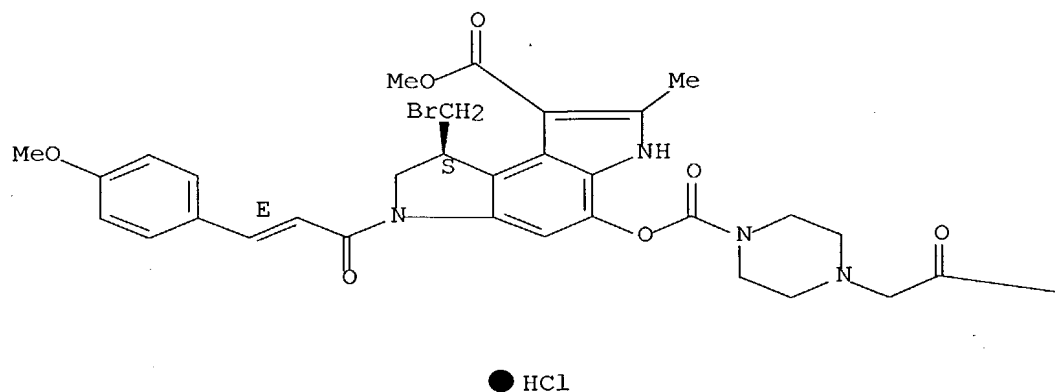
Absolute stereochemistry.
 Double bond geometry as shown.



● HCl

RN 186760-08-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-[2-(1-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrochloride, [S-(E)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

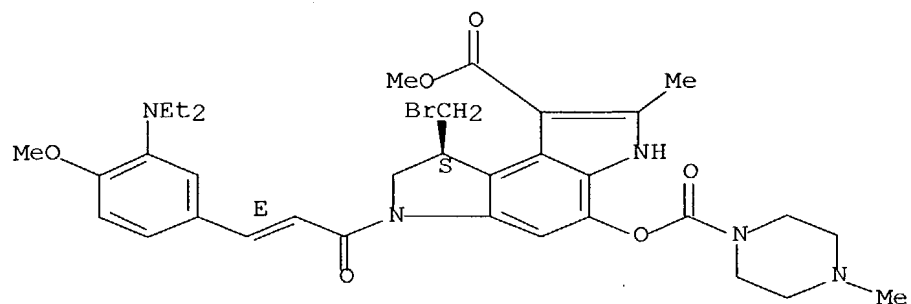


—NHPr-i

RN 186760-09-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



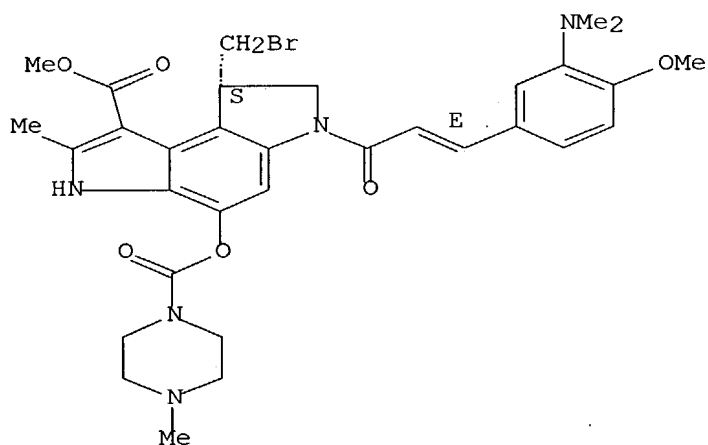
●2 HCl

RN 186760-10-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

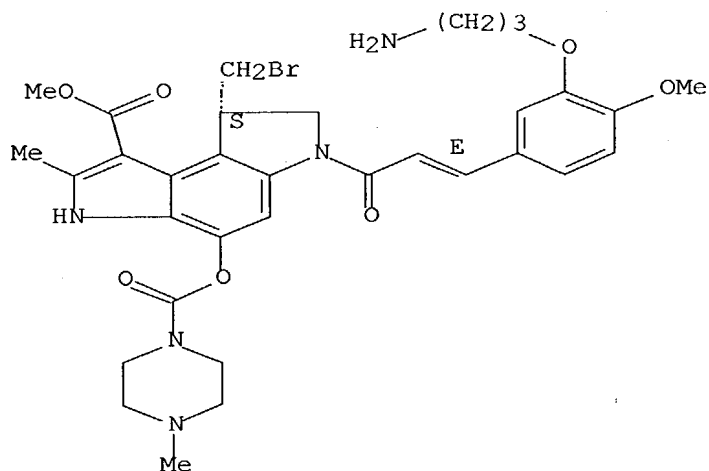
● HCl

RN 186760-11-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-[3-(3-aminopropoxy)-4-methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

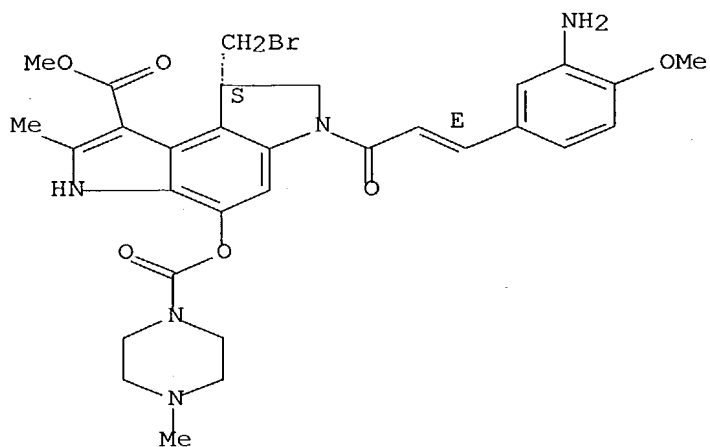
● 2 HCl

RN 186760-12-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



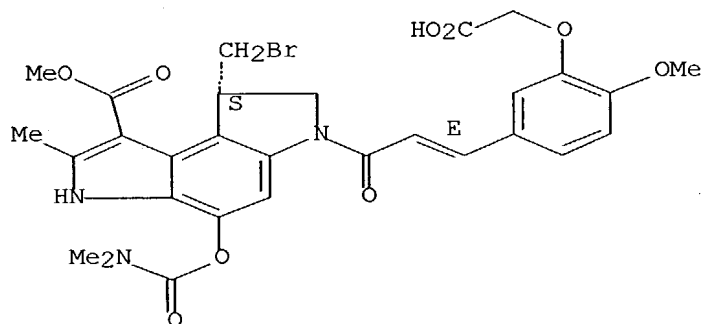
PAGE 2-A

● 2 HCl

RN 186760-21-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(carboxymethyl)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, [8aS-[2(E),7bS*,8aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L10 ANSWER 60 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:118877 CAPLUS Full-text
DN 126:131272
TI Total Synthesis of (+)-Duocarmycin A and epi-(+)-Duocarmycin A and Their
Unnatural Enantiomers: Assessment of Chemical and Biological Properties
AU Boger, Dale L.; McKie, Jeffrey A.; Nishi, Takahide; Ogiku, Tsuyoshi
CS Department of Chemistry, Scripps Research Institute, La Jolla, CA,
92037,
USA
SO Journal of the American Chemical Society (1997), 119(2), 311-325
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Full details of an enantioselective total synthesis of (+)-duocarmycin A are described in which a solution to the control of the relative and absolute stereochem. of the remote stereocenters is provided. Catalytic asym. dihydroxylation of propene I was employed to introduce the absolute stereochem. required for the activated cyclopropane, and a diastereoselective Dieckmann-type condensation of nitrile II was employed to control the absolute stereochem. of the C6 quaternary center. The complementary diastereoselectivity of a thermodyn. vs. kinetic condensation of II permitted the divergent synthesis of (+)-duocarmycin A or epi-(+)-duocarmycin A from common intermediates. Final introduction of the reactive cyclopropane was accomplished by transannular spirocyclization of the mesylate III upon treatment with base or directly from the corresponding free alc. itself, duocarmycin D1, upon Mitsunobu activation. Notably, the asym. dihydroxylation of I employing (DHQD)2-PHAL/(DHQ)2-PHAL was found to proceed with a reverse enantioselectivity than predicted from established models. Employing this approach, the key partial structures (+)-N-BOC-DA and (+)-6-epi-N-BOC-DA and their unnatural enantiomers were also prepared, and a study of their acid-catalyzed solvolysis reactivity, regioselectivity (3:2), and stereochem. is detailed. Notably, the solvolysis reaction regioselectivity is lower than the characteristic adenine N3 alkylation of duplex DNA, which proceeds with exclusive nucleophilic addition to the least substituted C8 cyclopropane carbon, and this may be attributed to the significant destabilizing torsional strain and steric interactions characteristic of the SN2 reaction of a large nucleophile that accompany the abnormal addition of adenine when restricted to the minor groove bound orientation of the reactants.

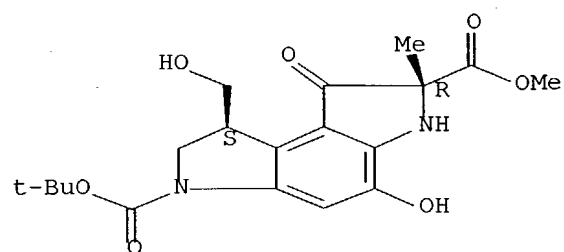
IT **181417-72-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and chemical and biol. properties of (+)-duocarmycin A and epi-(+)-duocarmycin A and their unnatural enantiomers)

RN 181417-72-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
2,3,7,8-tetrahydro-4-hydroxy-8-(hydroxymethyl)-2-methyl-1-oxo-,
6-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 61 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:604556 CAPLUS Full-text

DN 125:292259

TI Examination of the role of the duocarmycin SA methoxy substituents: identification of the minimum, fully potent DNA binding subunit

AU Boger, Dale L.; Bollinger, Bernd; Johnson, Douglas S.

CS Department Chemistry, Scripps Research Institute, La Jolla, CA, 92037, USA

SO Bioorganic & Medicinal Chemistry Letters (1996), 6(18), 2207-2210
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

DT Journal

LA English

AB Several analogs of duocarmycin SA were prepared and evaluated for DNA alkylating and cytotoxic activity in order to determine the role of the 3 methoxy substituents in biol. activity. The C5 methoxy substituent of the 5,6,7-trimethoxyindole subunit of duocarmycin SA was found to be necessary and sufficient for observation of the full potency of the natural product.

IT **182957-21-7P 182957-22-8P 182957-23-9P**
182957-24-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

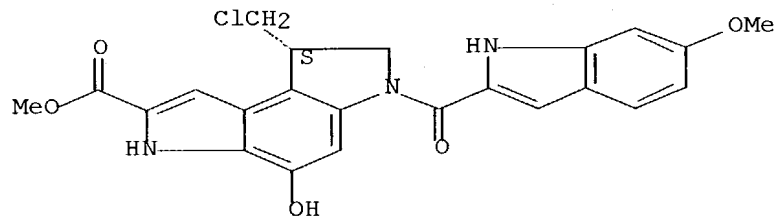
(Reactant or reagent)

(intermediate; role of duocarmycin SA methoxy substituents in DNA alkylating and cytotoxic activity)

RN 182957-21-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(6-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

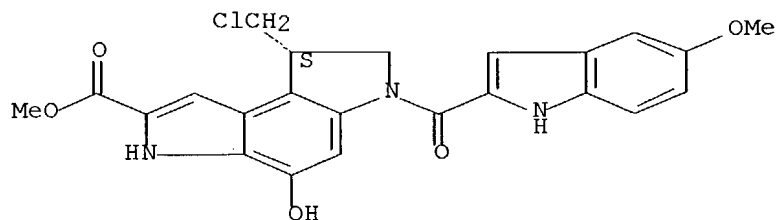
Absolute stereochemistry. Rotation (-).



RN 182957-22-8 CAPLUS

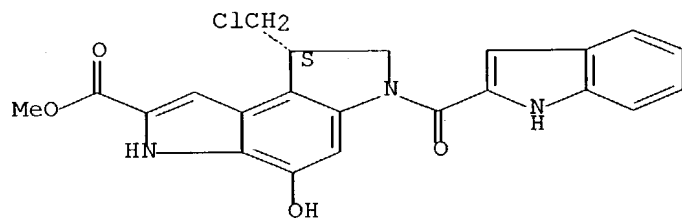
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



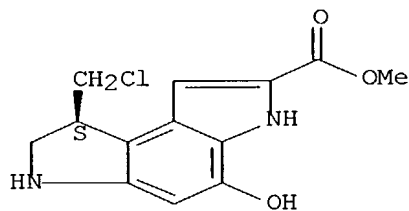
RN 182957-23-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-(1H-indol-2-ylcarbonyl)-, methyl ester, (8S)-
 (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 182957-24-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



● HCl

IT 182957-20-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

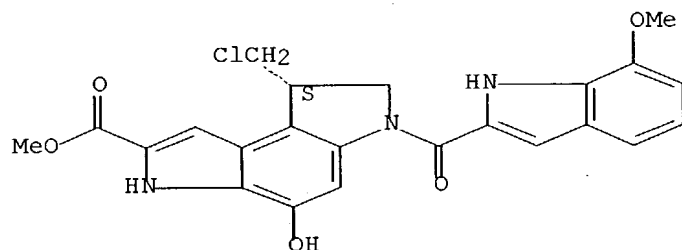
(Reactant or reagent)

(reactant; role of duocarmycin SA methoxy substituents in DNA
alkylating and cytotoxic activity)

RN 182957-20-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(7-methoxy-1H-indol-2-yl)carbonyl]-, methyl
ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 62 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:596991 CAPLUS Full-text

DN 125:328342

TI Synthesis and antitumor activity of duocarmycin derivatives:
modification

of segment A of duocarmycin B2

AU Nagamura, Satoru; Asai, Akira; Kanda, Yutaka; Kobayashi, Eiji; Gomi,
Katsushige; Saito, Hiromitsu

CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Tokyo, 194, Japan

SO Chemical & Pharmaceutical Bulletin (1996), 44(9), 1723-1730

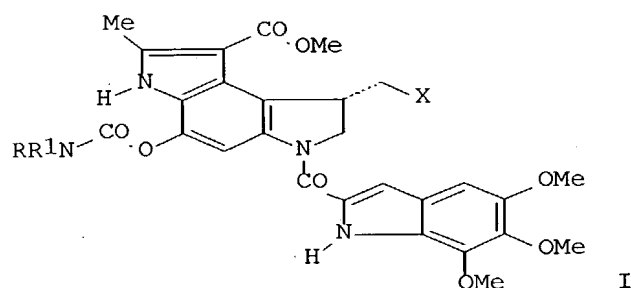
CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

GI



AB Several A-ring pyrrole derivs. of duocarmycin B2, e.g. I (RR1N = Me2N, 4-Me-piperazinyl, piperidinyl, pyrrolidinyl, X = Br, Cl), were synthesized from the 3-hydroxy compds. by utilizing an interesting acid-catalyzed rearrangement, their anticellular activity was preliminarily evaluated by assays of growth inhibition of HeLa S3 cells (in vitro) and antitumor activity against murine sarcoma 180 (in vivo). The 8-O-N,N-dialkylcarbamoyl derivs. of the A-ring pyrrole compound showed remarkably potent in vivo antitumor activity, superior to that of duocarmycin B2. These derivs. were subjected to further biol. evaluation. They exhibited potent antitumor activity toward murine solid tumors including M5076 sarcoma, B-16 melanoma and Colon 26 adenocarcinoma. Their most noteworthy feature was their efficacy against various human xenografts including LC-6 (lung), St-4 (stomach), and Co-3 (colon).

IT 171599-25-0 171599-29-4

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological

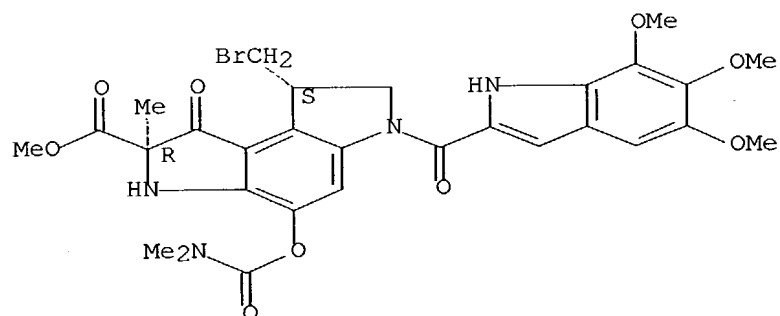
study, unclassified); BIOL (Biological study)

(synthesis and antitumor activity of duocarmycin derivs.)

RN 171599-25-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl] oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (2R-trans)-
(9CI) (CA INDEX NAME)

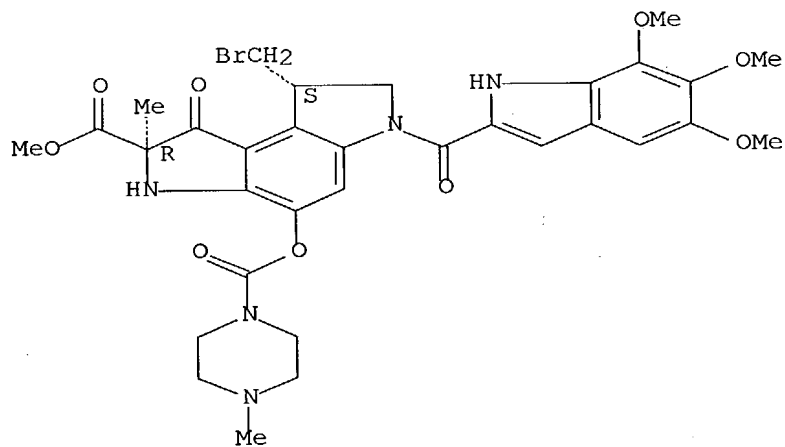
Absolute stereochemistry.



RN 171599-29-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-
 piperazinyl) carbonyl]oxy]-1-
 oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester,
 monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



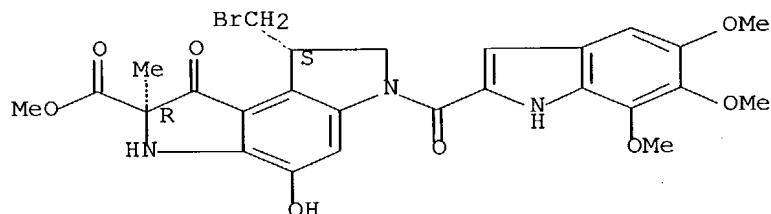
PAGE 2-A

● HCl

IT 124325-94-6, Duocarmycin B2

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); RCT (Reactant); BIOL (Biological study); RACT
 (Reactant or reagent)
 (synthesis and antitumor activity of duocarmycin derivs.)
 RN 124325-94-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
 indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

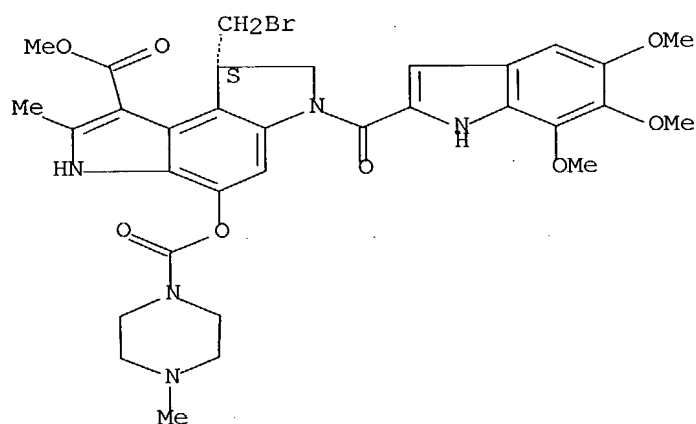
Absolute stereochemistry.



IT 154889-68-6P 160819-28-3P 177958-19-9P
 177958-20-2P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
 (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis and antitumor activity of duocarmycin derivs.)
 RN 154889-68-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
 tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
 INDEX
 NAME)

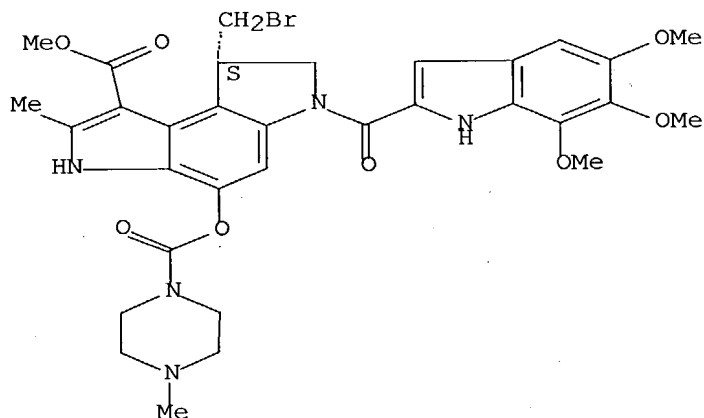
Absolute stereochemistry.



RN 160819-28-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, monohydrobromide, (8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

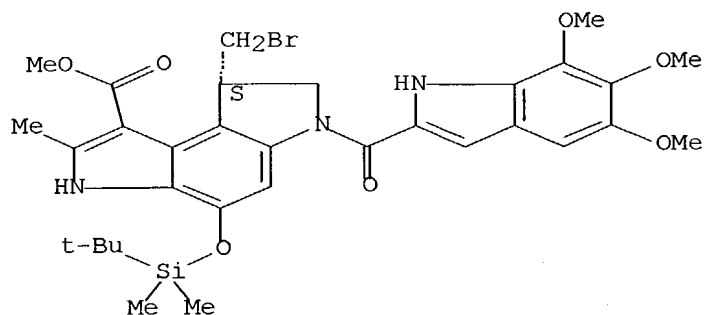


PAGE 2-A

● HBr

RN 177958-19-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



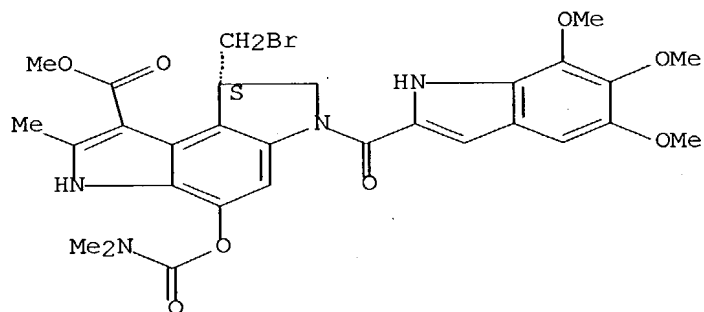
RN 177958-20-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



IT 154715-68-1P 183240-24-6P 183240-25-7P
183240-26-8P 183240-27-9P 183240-28-0P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)

(synthesis and antitumor activity of duocarmycin derivs.)

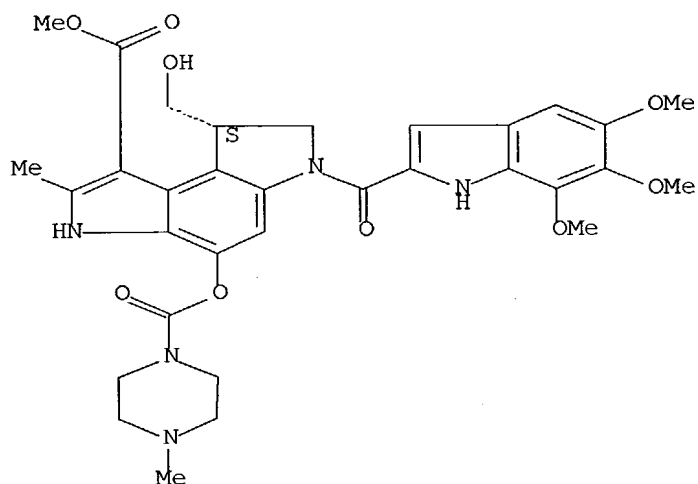
RN 154715-68-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-
(hydroxymethyl)-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-
[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (S)- (9CI)

(CA

INDEX NAME)

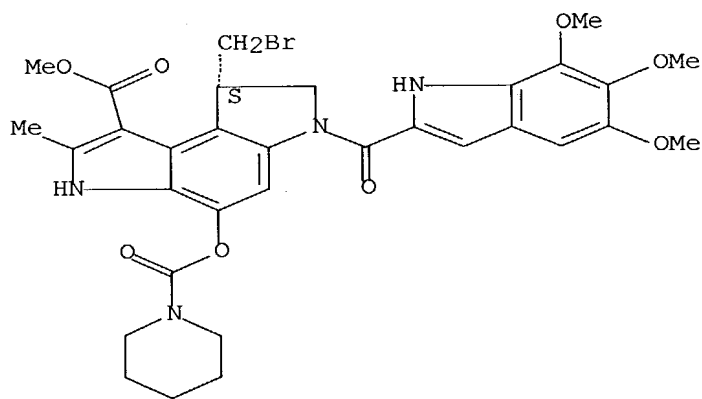
Absolute stereochemistry.



RN 183240-24-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

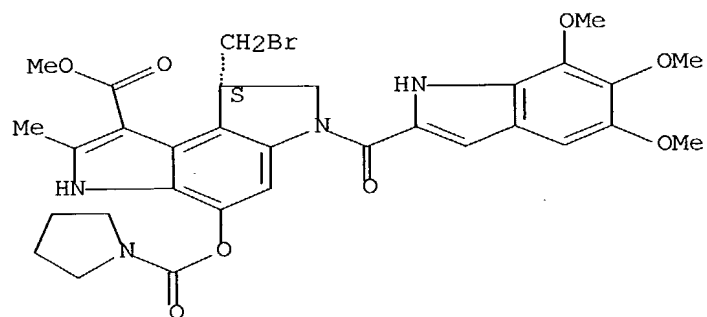
Absolute stereochemistry.



RN 183240-25-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

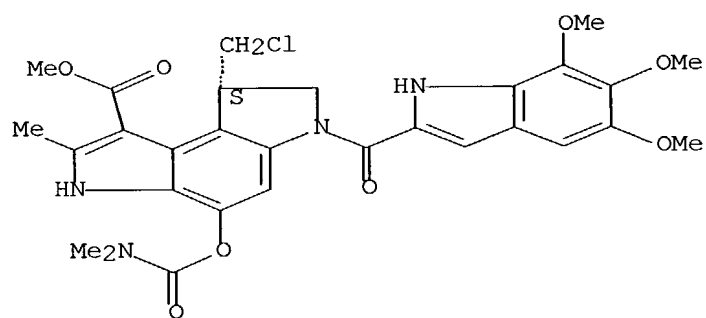
Absolute stereochemistry.



RN 183240-26-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[(dimethylamino) carbonyl] oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

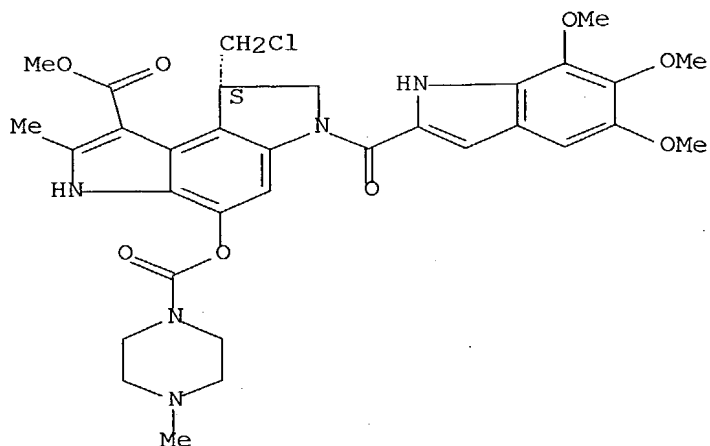


RN 183240-27-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl] oxy]-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, monohydrochloride,
 (S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

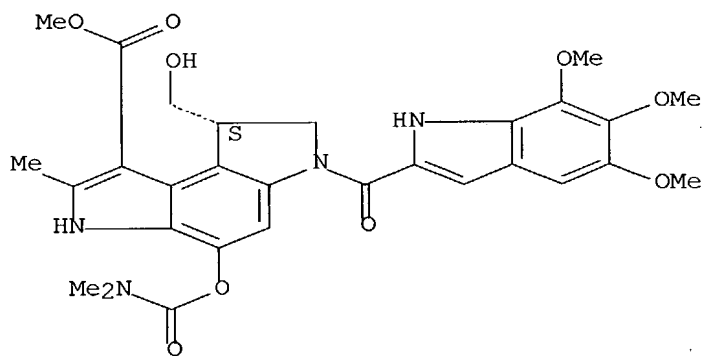


PAGE 2-A

● HCl

RN 183240-28-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-
[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-
methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 129953-15-7P 129953-17-9P 183240-30-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT

(Reactant or reagent)

(synthesis and antitumor activity of duocarmycin derivs.)

RN 129953-15-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-

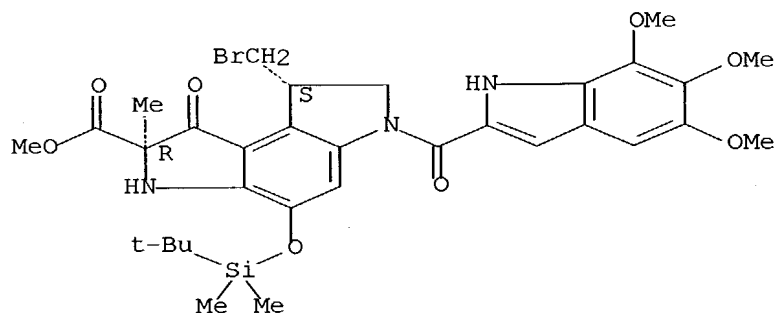
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-

(9CI)

(CA INDEX NAME)

Absolute stereochemistry.



RN 129953-17-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(1,1-

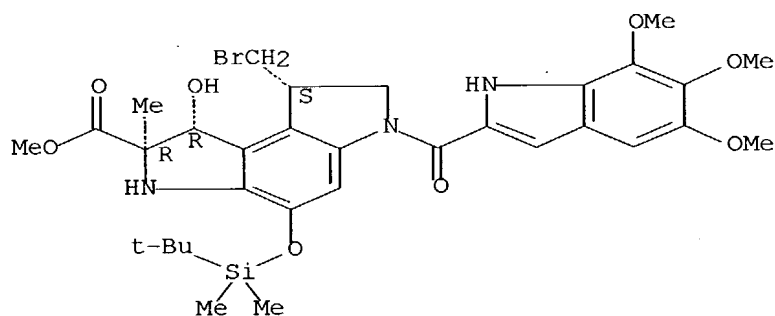
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-

methyl-

6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 183240-30-4 CAPLUS

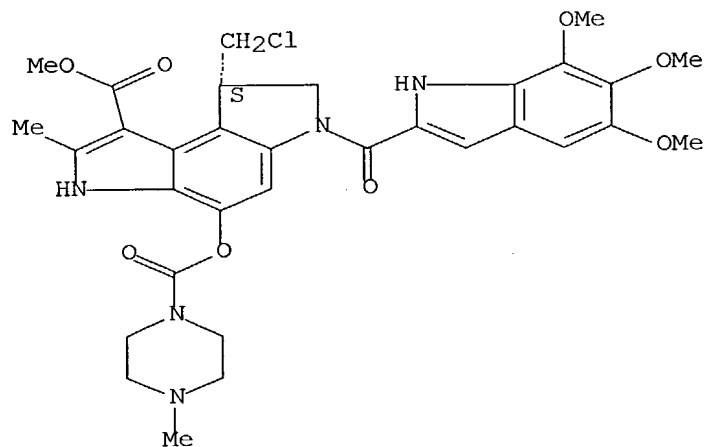
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-

3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.



IT 183388-25-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and antitumor activity of duocarmycin derivs.)

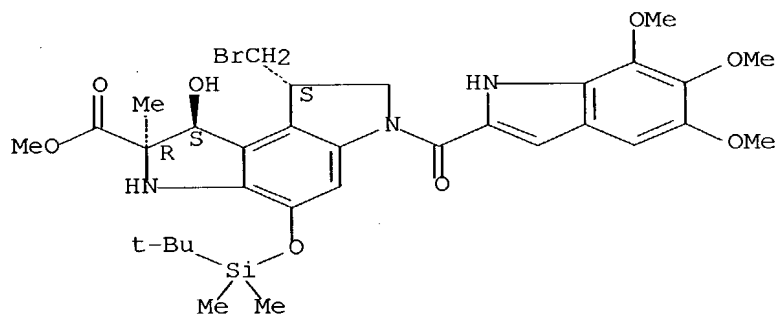
RN 183388-25-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

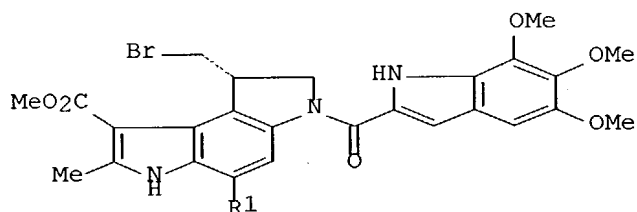
[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-

6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2S,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 63 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:572393 CAPLUS Full-text
 DN 125:300656
 TI Synthesis and antitumor activity of duocarmycin derivatives: A-ring
 pyrrole analogs of duocarmycin B2
 AU Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
 CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Machida, 194, Japan
 SO Bioorganic & Medicinal Chemistry (1996), 4(8), 1379-1391
 CODEN: BMECEP; ISSN: 0968-0896
 PB Elsevier
 DT Journal
 LA English
 GI



I

AB A series of the eight-substituted A-ring pyrrole derivs. of duocarmycin B2 I [R = H, Me; R1 = PhCH2O, MeO, Me2N(CH2)2O, MeSO2O, F3CSO2O, H, NC, AcO, HCl.MeN(CH2)2N(CH2)2CO(CH2)3CO2, MeO2CO, PhO2CO, PhCH2O2CCH2NHCO2, HO2CCH2NHCO2, L-Phe-O, PhNHCO2, 4-MeOC6H4NHCO2, HCl.Me2CHNHCOCH2N(CH2)2N(CH2)2CO2, HCl.(CH2)5N(CH2)5NCO2, HO2CCH2N(Me)CO2, MeN(CH2)2N(CH2)2CO2] were synthesized, and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. In addition, the stability of the analogs in aqueous solution was examined I (R = H, R1 = H, NC) which cannot structurally release the cyclopropane compound (DU-86), exhibited extremely diminished anticellular activity compared with duocarmycin A or DU-86. The ethers and the sulfonates which were not converted to DU-86 under usual conditions (35°C, pH 7), showed almost equal in vivo activities to that of duocarmycin A. However, their optimal doses were significantly higher than that for duocarmycin A. Most of the A-ring pyrrole analogs which can be chemical or enzymically converted to DU-86, displayed remarkably superior in vivo antitumor activity to duocarmycin A. These results suggest that the a-ring pyrrole analogs need to chemical or enzymically release DU-86 as an active metabolite to exhibit potent in vivo antitumor activity.

IT 182360-43-6P 182360-56-1P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological

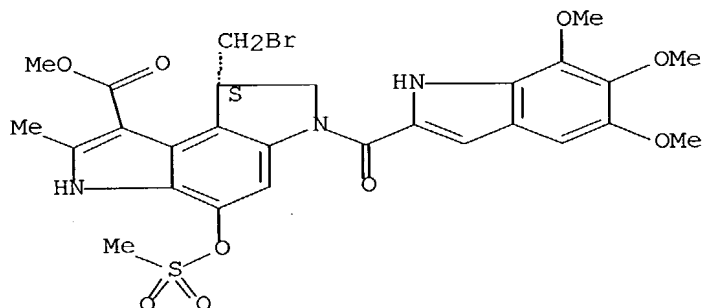
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
 (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis and antitumor activity of A-ring pyrrole analogs of
 duocarmycin B2)

RN 182360-43-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(methylsulfonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

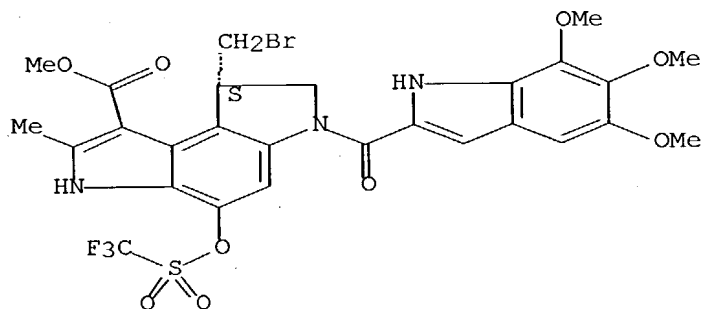
Absolute stereochemistry.



RN 182360-56-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[trifluoromethylsulfonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 168776-83-8P 182360-42-5P 182360-48-1P
182360-49-2P 182360-50-5P 182360-52-7P
182360-55-0P 182360-60-7P 182360-61-8P
182360-63-0P 182360-65-2P 182360-66-3P
182360-67-4P 182360-68-5P 182578-89-8P

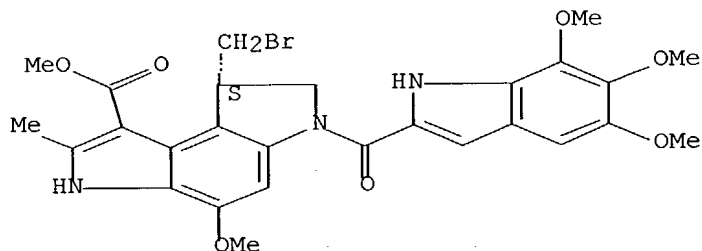
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of A-ring pyrrole analogs of duocarmycin B2)

RN 168776-83-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-
 , methyl ester, (S)- (9CI) (CA INDEX NAME)

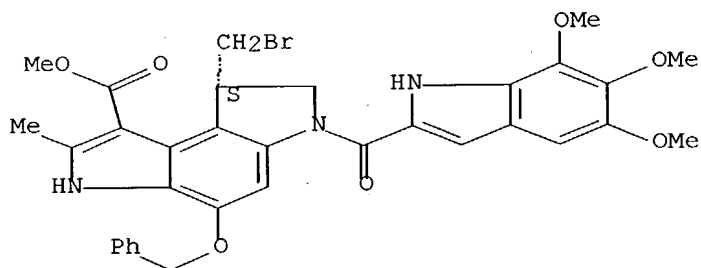
Absolute stereochemistry. Rotation (-).



RN 182360-42-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

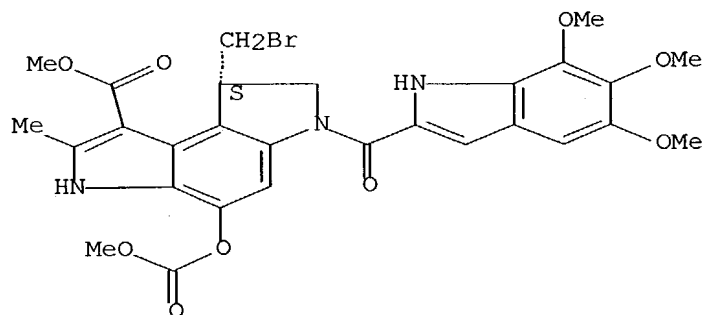
Absolute stereochemistry.



RN 182360-48-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

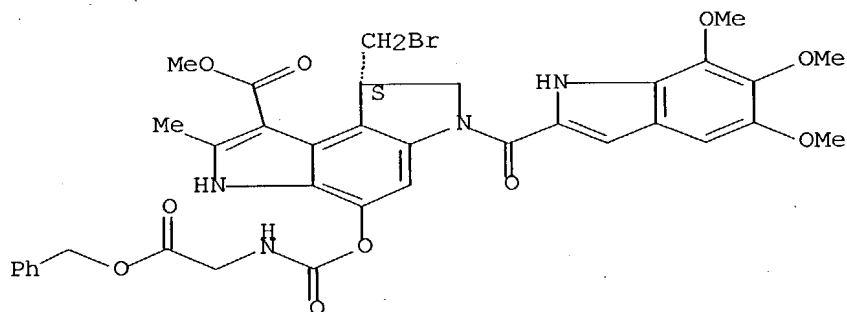
Absolute stereochemistry.



RN 182360-49-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI)
(CA INDEX NAME)

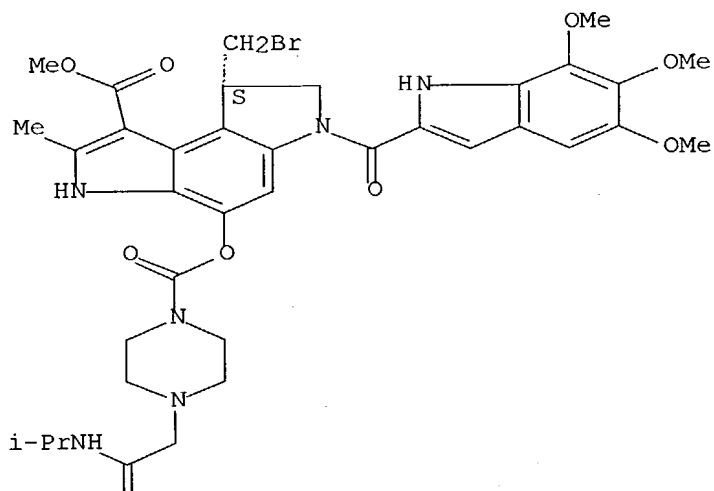
Absolute stereochemistry.



RN 182360-50-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-[2-[(1-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

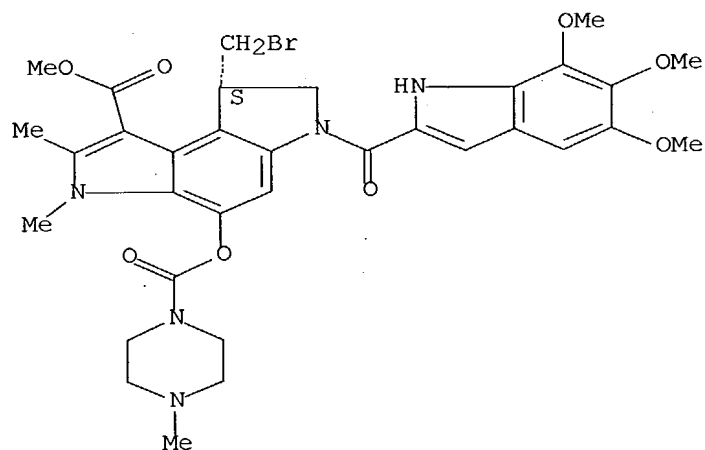


U

● HCl

RN 182360-52-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2,3-dimethyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI)
 (CA INDEX NAME)

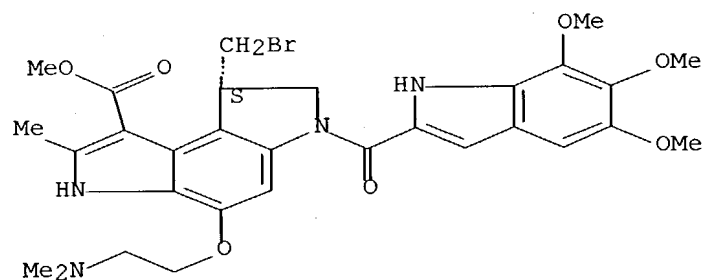
Absolute stereochemistry.



RN 182360-55-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[2-(dimethylamino)ethoxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

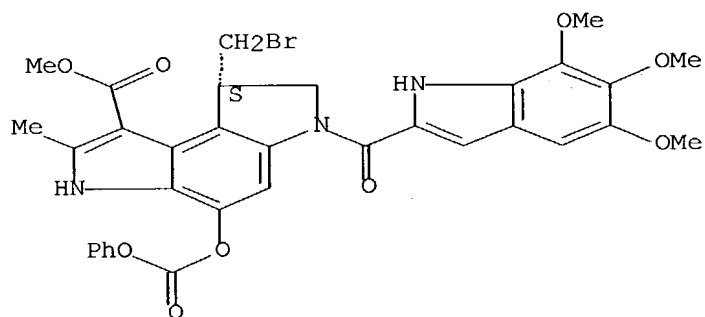
Absolute stereochemistry.



RN 182360-60-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(phenoxy-carbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

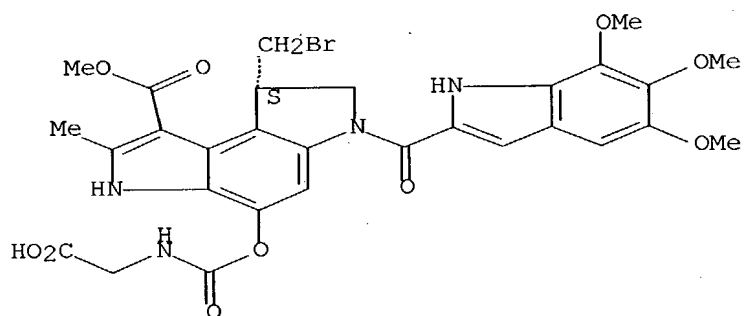
Absolute stereochemistry.



RN 182360-61-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, (S)- (9CI)
(CA INDEX NAME)

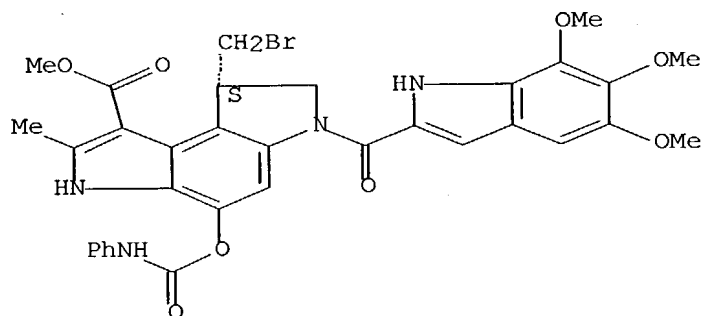
Absolute stereochemistry.



RN 182360-63-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(phenylamino)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

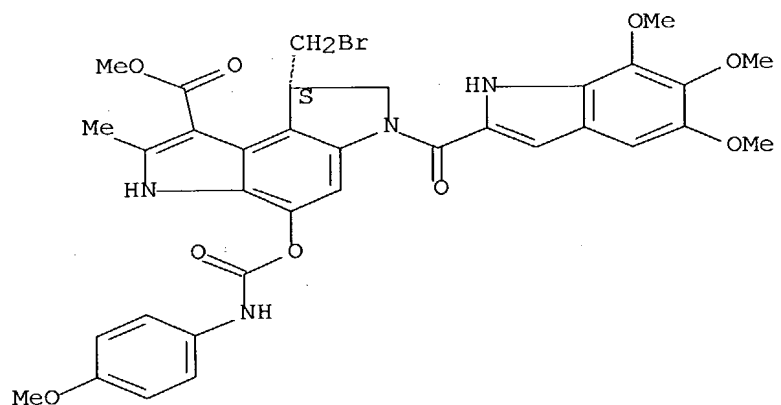
Absolute stereochemistry.



RN 182360-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[(4-methoxyphenyl)amino]carbonyl]oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



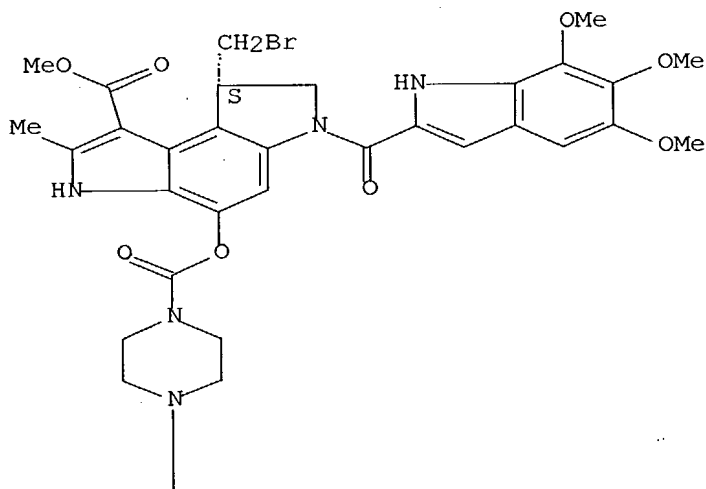
RN 182360-66-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-(1-piperidinyl)-1-piperazinyl]carbonyl]oxy]-

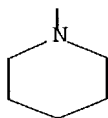
6-

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



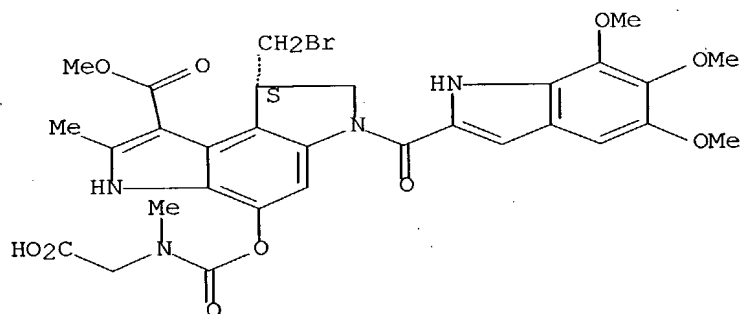
PAGE 1-A



● HCl

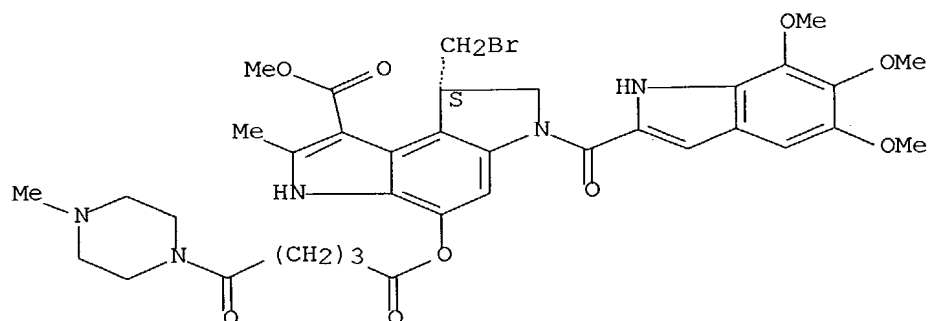
RN 182360-67-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 6- [[[carboxymethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, (S)- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 182360-68-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
 6- tetrahydro-2-methyl-4-[[5-(4-methyl-1-piperazinyl)-1,5-dioxopentyl]oxy]-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
 monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

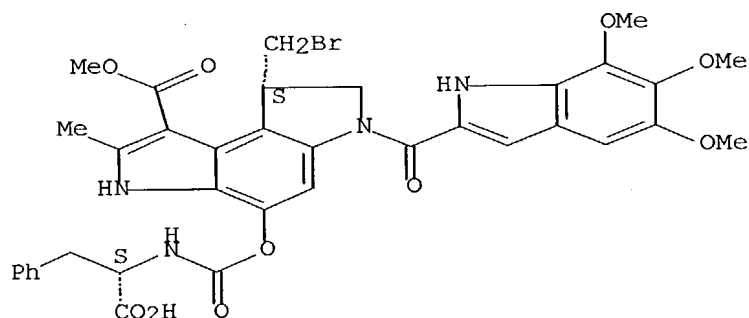


● HCl

RN 182578-89-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1-carboxy-2-phenylethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, [S-(R*,R*)]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154715-66-9P 182360-41-4P 182360-45-8P

182360-53-8P 182360-54-9P 182360-58-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

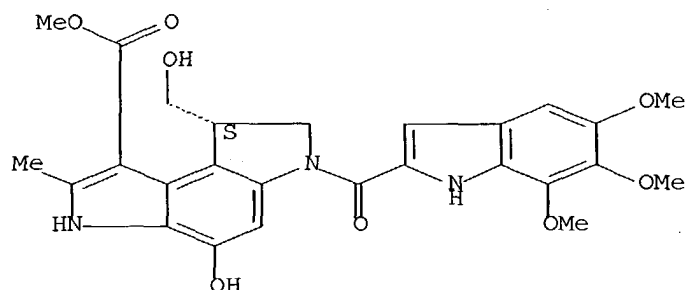
(Reactant or reagent)

(synthesis and antitumor activity of A-ring pyrrole analogs of duocarmycin B2)

RN 154715-66-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-4-hydroxy-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

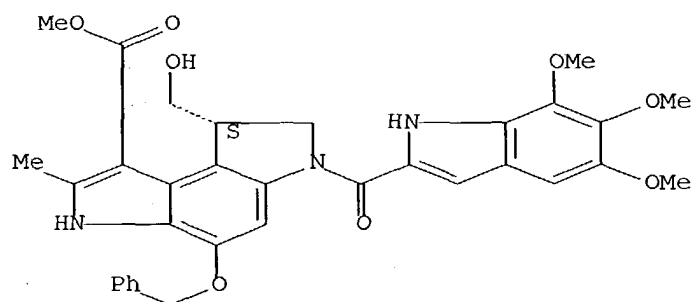
Absolute stereochemistry.



RN 182360-41-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

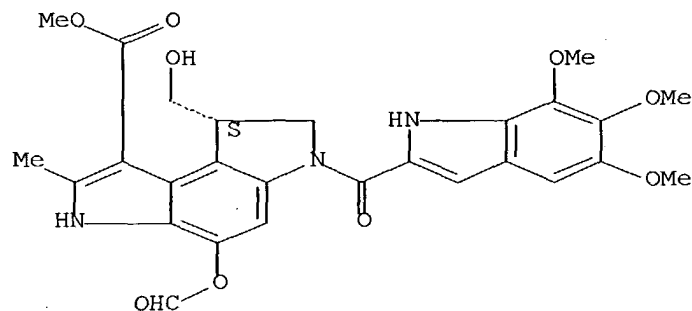
Absolute stereochemistry.



RN 182360-45-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(formyloxy)-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

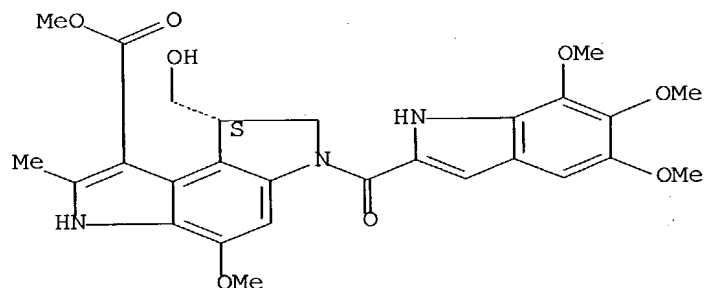
Absolute stereochemistry.



RN 182360-53-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

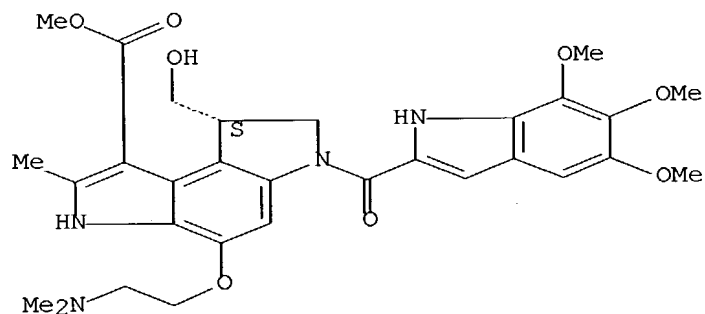


RN 182360-54-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[2-(dimethylamino)ethoxy]-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI)

(CA INDEX NAME)

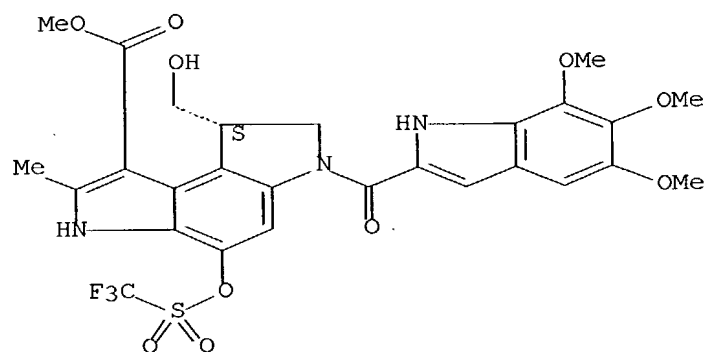
Absolute stereochemistry.



RN 182360-58-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[(trifluoromethyl)sulfonyloxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **182360-47-0P**

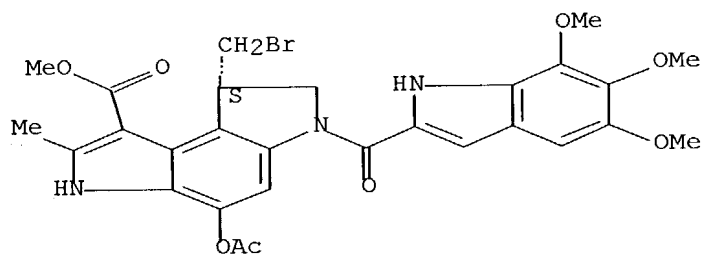
RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and antitumor activity of A-ring pyrrole analogs of
duocarmycin B2)

RN 182360-47-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-
(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-
2-
yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 64 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:551110 CAPLUS Full-text
 DN 125:195630
 TI Preparation of bis(pyrroloindole) derivatives as antitumor and
 antibacterial agents
 IN Fukuda, Yasumichi; Oomori, Yasuo; Ko, Hiroyuki; Terajima, Atsuro
 PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
 SO Jpn. Kokai Tokkyo Koho, 10 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08151379	A2	19960611	JP 1994-295275	19941129
PRAI	JP 1994-295275		19941129		
OS	MARPAT 125:195630				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [X1, X2 = NH, etc.; Y1, Y2 = H, etc.; R =
 heterocyclic ring described by a generic structure] are prepared The
 title compound II (preparation given) in vitro showed IC50 of 32 ng/mL
 against HeLaS3 cells.

IT **180910-74-1P**

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
 use);

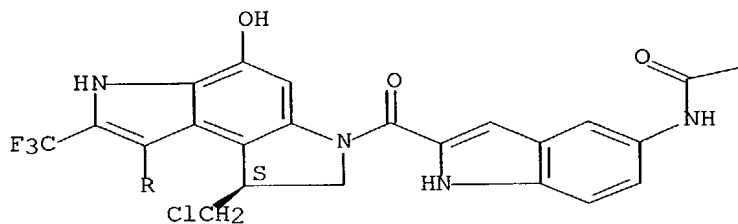
BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of bis(pyrroloindole) derivs. as antitumor and
 antibacterial
 agents)

RN 180910-74-1 CAPLUS

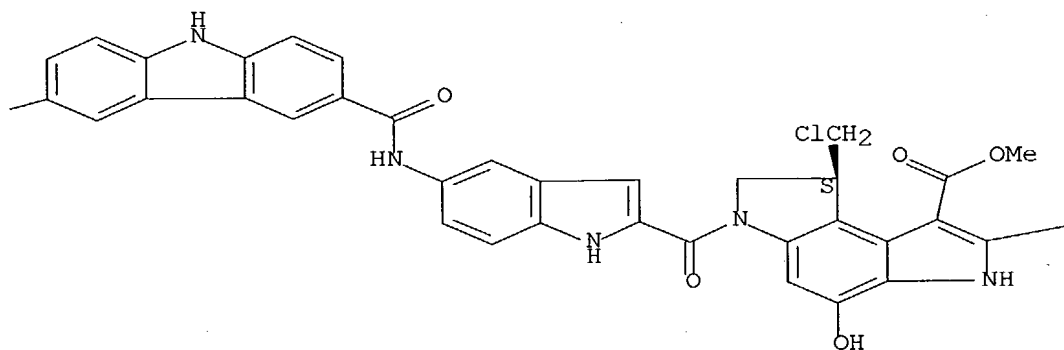
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[9H-carbazole-3,6-
 diylbis(carbonylimino-1H-indole-5,2-diylcarbonyl)]bis[8-(chloromethyl)-
 3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester,
 [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



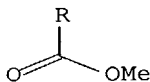
PAGE 1-B



PAGE 1-C

—CF₃

PAGE 2-A



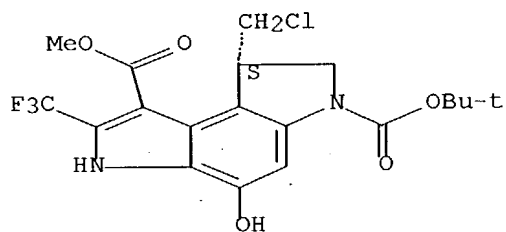
IT 157904-28-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bis(pyrroloindole) derivs. as antitumor and
antibacterial agents)

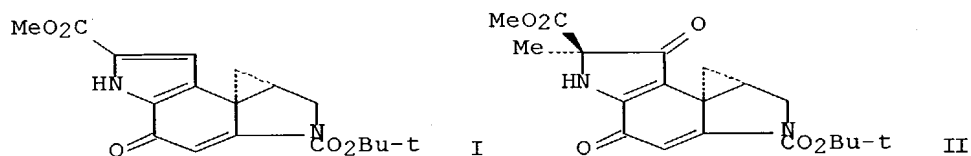
RN 157904-28-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 65 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:545200 CAPLUS Full-text
 DN 125:221416
 TI A comparative study of the solvolysis reactivity, regioselectivity, and stereochemistry of the duocarmycin A and SA alkylation subunits
 AU Boger, Dale L.; Goldberg, Joel; McKie, Jeffrey A.
 CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
 SO Bioorganic & Medicinal Chemistry Letters (1996), 6(16), 1955-1960
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier
 DT Journal
 LA English
 GI



AB The comparative solvolysis reactivity, regioselectivity, and stereochem. of N-BOC-DSA (I) and N-BOC-DA (II), simple derivs. of the DNA alkylation subunits of duocarmycin SA and A, are detailed. Most important of the observations is the substantially greater reactivity of II vs. I (16x), the modest regioselectivity of both I (6.5-4:1) and II (1.5:1), and the establishment that the abnormal ring expansion solvolysis proceeds by SN2 addition to the activated cyclopropane with clean inversion of the reacting center stereochem.

IT 144732-55-8P 181417-69-6P 181417-72-1P

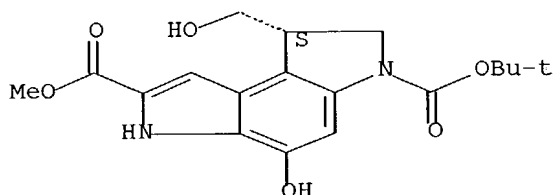
RL: SPN (Synthetic preparation); PREP (Preparation)

(reactivity, regioselectivity, and stereochem. of the solvolysis of the duocarmycin A and SA alkylation subunits)

RN 144732-55-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid, 1,6-dihydro-5-hydroxy-1-(hydroxymethyl)-, 3-(1,1-dimethylethyl) 7-methyl ester, (S)- (9CI) (CA INDEX NAME)

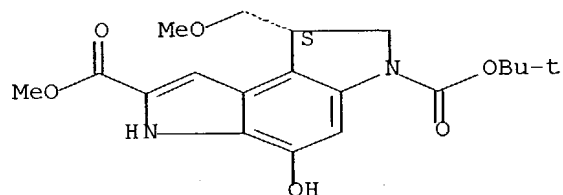
Absolute stereochemistry.



RN 181417-69-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
7,8-dihydro-4-hydroxy-8-(methoxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

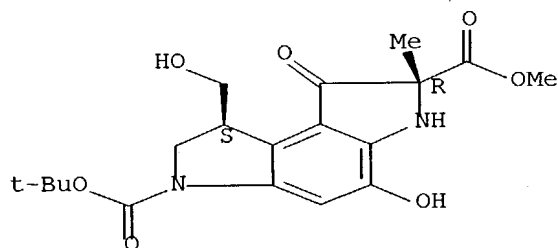
Absolute stereochemistry.



RN 181417-72-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
2,3,7,8-tetrahydro-4-hydroxy-8-(hydroxymethyl)-2-methyl-1-oxo-,
6-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 66 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:531603 CAPLUS Full-text

DN 125:167964

TI Preparation of bis(trifluoromethylpyrroloindolecarboxylic acid) and bis(trifluoromethylcyclopropapyrroloindolecarboxylic acid) derivatives as antitumor agents

IN Fukuda, Yasumichi; Furuta, Kosuke; Oomori, Yasuo; Ko, Hiroyuki; Terajima,

Atsuro

PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res

SO Jpn. Kokai Tokkyo Koho, 16 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08151380	A2	19960611	JP 1994-295276	19941129
PRAI	JP 1994-295276		19941129		
OS	MARPAT 125:167964				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I and II; R = linear or branched C1-6 alkyl; R1 = Q - Q4; wherein Z = NHCO-R3-CONH, NH, O, (CH2)n (n = 0-4), (CH:CH)m, (C.tplbond.C)m (m = 1,2), X3-(CH2)n-X3; or Z = NHCONH and X3 = O; wherein R3 = Q5, Q6; X1, X2, X4, X5 = H, OH, linear or branched C1-6 alkyl, alkyloxy, or alkyloxycarbonyl, (un)substituted aryloxy; X3 = NH, O; R2 = H, HO-protecting group, substituent hydrolyzable in vivo; Y = halo, arylsulfonyloxy, lower alkylsulfonyloxy, haloalkylsulfonyloxy, N3] and optically active isomers and pharmacol. acceptable salts thereof, which have low toxicity and potent and highly selective antitumor activity against solid tumors, even those with reduced sensitivity for anticancer agents, and also show antibacterial activity, are prepared Thus, Me (S)-tert-butoxycarbonyl-1-chloromethyl-5-hydroxy-7-trifluoromethyl-1,2,3,6-tetrahydropyrrolo[3,2-e]indole-8-carboxylate was stirred with 3 M HCl/EtOAc at room temperature for 40 min and after distilling off the solvent, treated with 5,5'-(carbonyldiimino)bisbenzofuran-2-carboxylic acid and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and stirred in DMF at room temperature overnight to give (S,S)-I [R = Me, R1 = Q (wherein Z = NHCONH, X1 = X2 = H, X3 = O), Y = Cl, R2 = H]. The latter compound and (S,S)-I [R = Me, R1 = Q (wherein Z = single bond, X1 = X2 = H, X3 = NH), Y = Cl, R2 = H] in vitro showed IC50 of 0.31 and 0.0049 ng/mL against Hela S3 cells and in vivo inhibited the growth of colon 26 tumor transplanted in mice by 92% at 0.0156 mg/kg and 84% at 0.000977 mg/kg, resp.

IT 180525-88-6P 180525-89-7P 180525-90-0P
180525-91-1P 180525-92-2P 180525-93-3P
180525-94-4P 180525-95-5P 180525-96-6P
180525-97-7P 180525-98-8P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

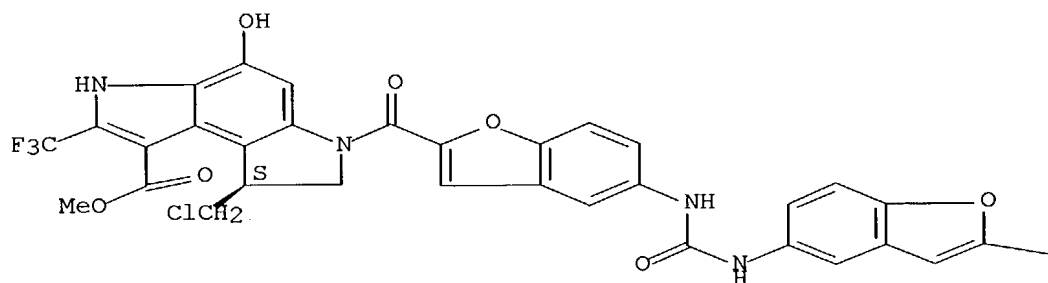
(preparation of bis(trifluoromethylpyrroloindolecarboxylic acid) and bis(trifluoromethylcyclopropapyrroloindolecarboxylic acid)derivs. as antitumor agents)

RN 180525-88-6 CAPLUS

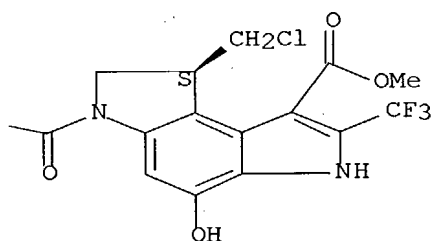
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[carbonylbis(imino-5,2-benzofurandiylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

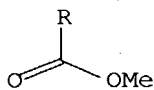
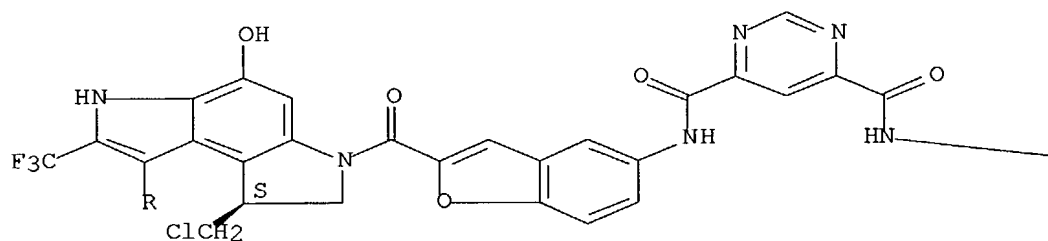


RN 180525-89-7 CAPLUS

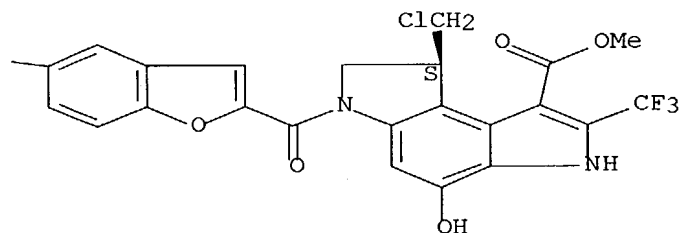
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[4,6-pyrimidinediylbis(carbonylimino-5,2-benzofurandiylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



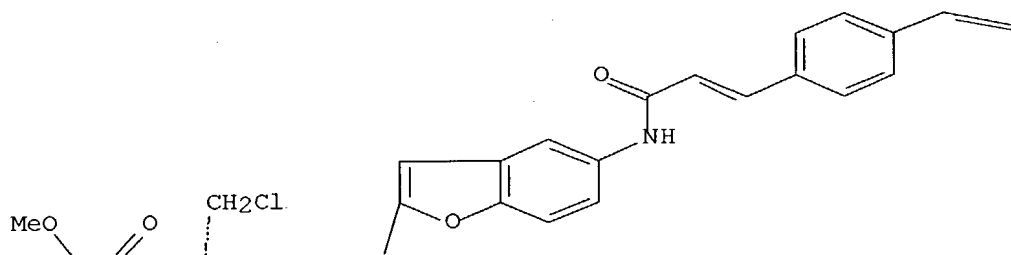
PAGE 1-B



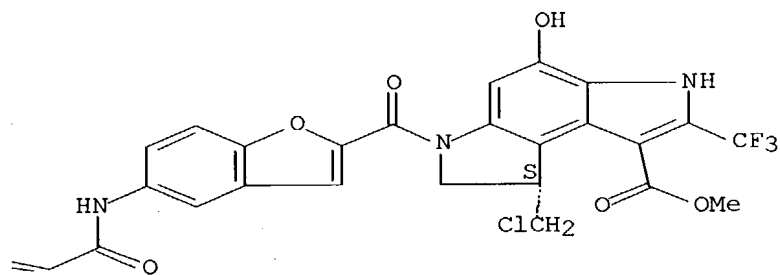
RN 180525-90-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-phenylenebis[(1-oxo-2-propene-3,1-diyl)imino-5,2-benzofurandiylcarbonyl]]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry unknown.

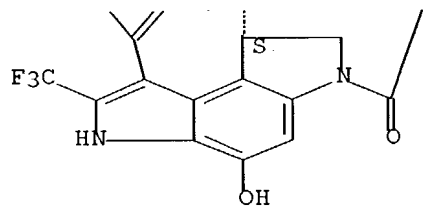
PAGE 1-A



PAGE 1-B



PAGE 2-A



RN 180525-91-1 CAPLUS

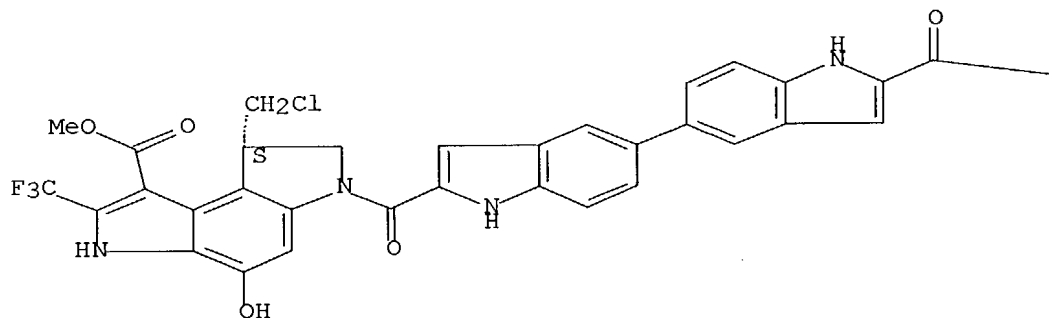
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-([5,5'-bi-1H-indole]-

2,2'-diyl dicarbonyl)bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-

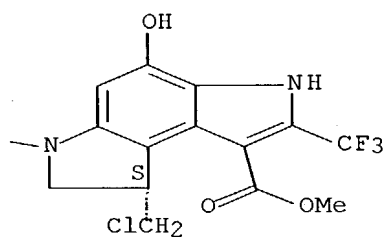
2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

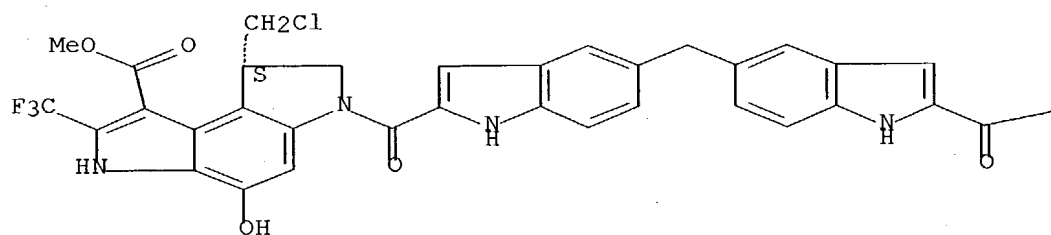


RN 180525-92-2 CAPLUS

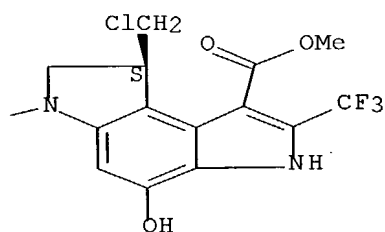
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[methylenebis(1H-indole-5,2-diyl carbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

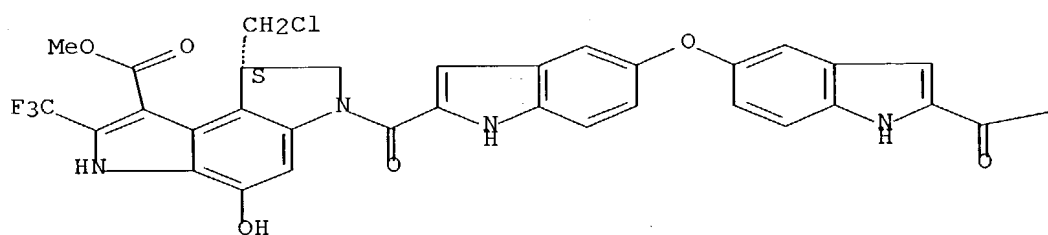


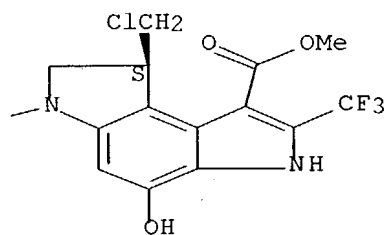
RN 180525-93-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[oxybis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A

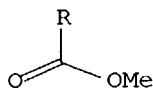
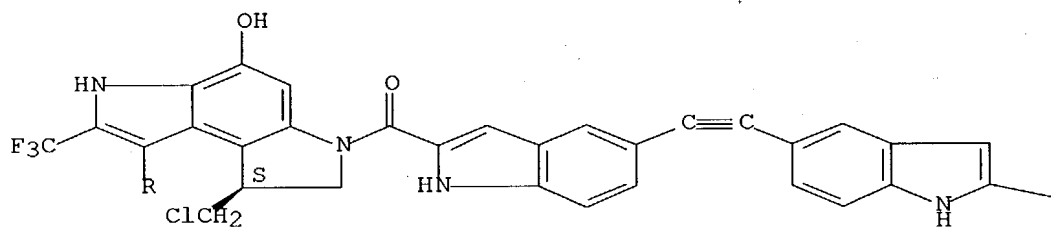


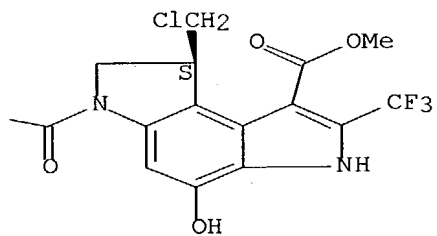


RN 180525-94-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,2-ethynediylbis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

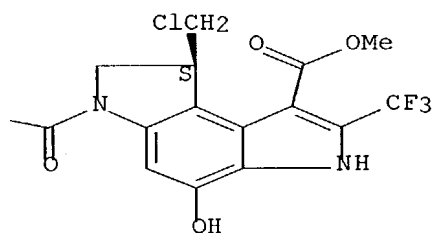
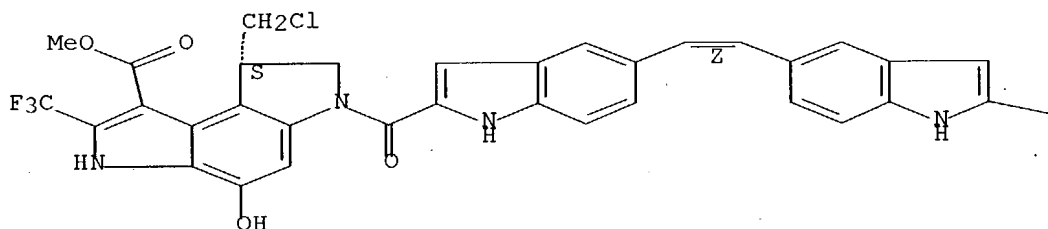
Absolute stereochemistry. Rotation (+).





RN 180525-95-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(1Z)-1,2-ethenediylbis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI)
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry as shown.

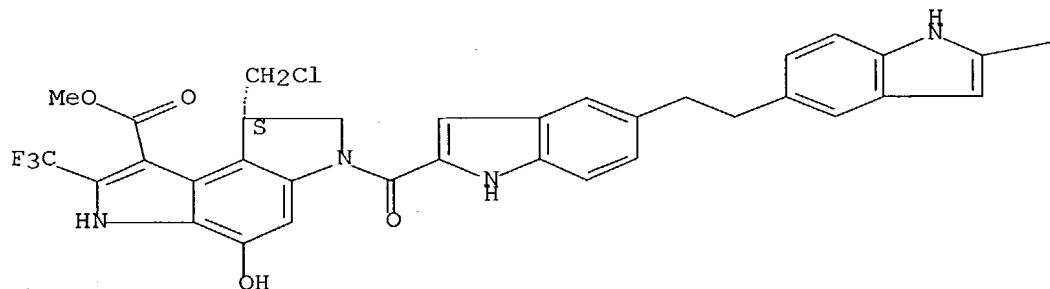


RN 180525-96-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,2-

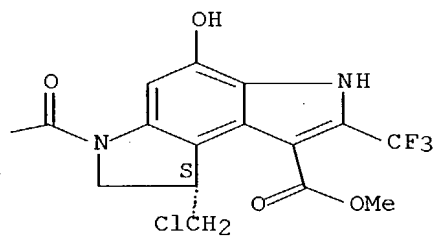
ethanediylbis(1H-indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A

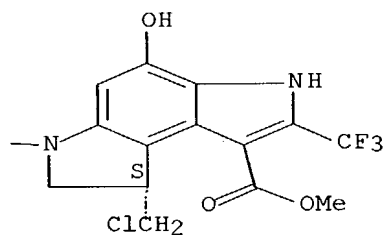
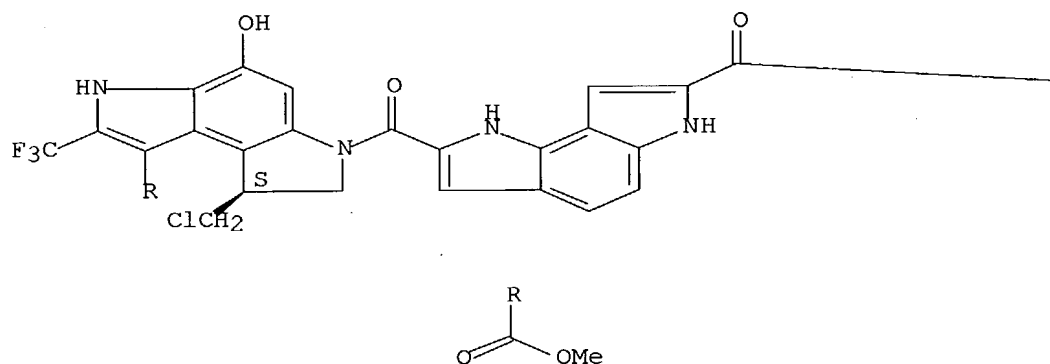


PAGE 1-B



RN 180525-97-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(1,6-dihydrobenzo[1,2-b:3,4-b']dipyrrole-2,7-diyl)dicarbonyl]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

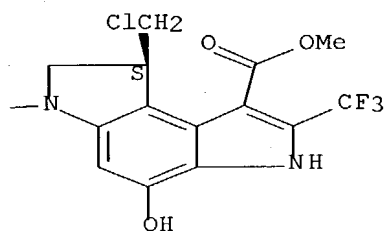
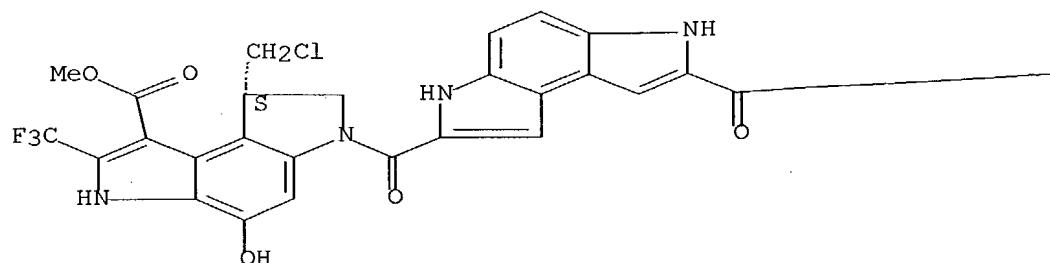
Absolute stereochemistry. Rotation (+).



RN 180525-98-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(3,6-dihydrobenzo[1,2-b:4,3-b']dipyrrole-2,7-diyl)dicarbonyl]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 157904-28-4

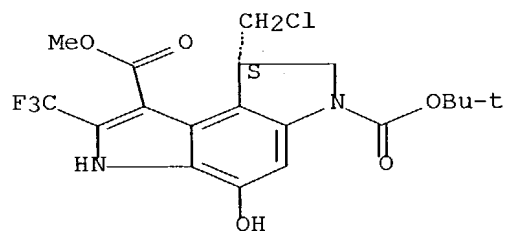
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of bis(trifluoromethylpyrroloindolecarboxylic acid) and bis(trifluoromethylcyclopropapyrroloindolecarboxylic acid)derivs. as antitumor agents)

RN 157904-28-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 67 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:483538 CAPLUS Full-text
 DN 125:142701
 TI Preparation of heterocyclic compounds as antitumor agents
 IN Fukuda, Yasumichi; Seto, Shigeki; Oomori, Yasuo; Ebisu, Hiroyuki;
 Terashima, Shiro
 PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center
 SO PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9616965	A1	19960606	WO 1995-JP2413	19951128
	W:	AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TM, TT, UA, US, UZ, VN			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	JP 08208653	A2	19960813	JP 1995-305851	19951124
	CA 2205872	AA	19960606	CA 1995-2205872	19951128
	AU 9539370	A1	19960619	AU 1995-39370	19951128
	AU 693283	B2	19980625		
	EP 799827	A1	19971008	EP 1995-937194	19951128
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE			
	CN 1174553	A	19980225	CN 1995-197472	19951128
	CN 1051552	B	20000419		
	HU 77654	A2	19980728	HU 1998-67	19951128
	TW 399053	B	20000721	TW 1996-85100362	19960111
	US 5786486	A	19980728	US 1997-849160	19970513
PRAI	JP 1994-295274	A	19941129		
	JP 1995-305851	A	19951124		
	WO 1995-JP2413	W	19951128		

OS MARPAT 125:142701

GI For diagram(s), see printed CA Issue.

AB The title compds. I [X1, X2 = H, halo, etc.; X1 may be linked to X2; ring A = pyrrole, benzene ring, etc.; R1, R2 = Q1, etc.; R4 = H, OH-protecting group, etc.; Y = halo, etc.; ring B = fused ring, etc.] are prepared. The title compound II (preparation given) in vitro showed IC50 of 0.0031 ng/mL against HeLa S3 cells.

IT 179693-47-1P 179693-48-2P 179693-49-3P
 179693-50-6P 179693-51-7P 179693-52-8P
 179693-53-9P 179693-54-0P 179693-55-1P
 179693-56-2P 179693-57-3P 179693-58-4P
 179693-59-5P 179693-60-8P 179693-61-9P
 179693-62-0P 179693-63-1P 179693-64-2P
 179693-67-5P 179693-68-6P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIO (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclic compds. as antitumor agents)

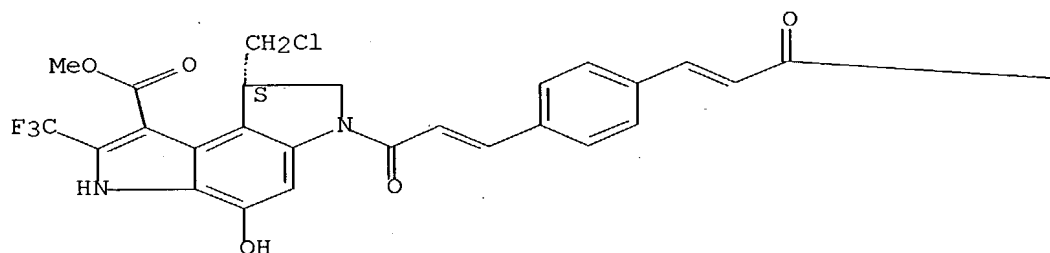
RN 179693-47-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-

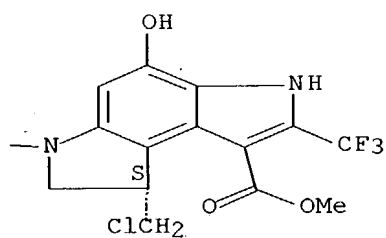
phenylenebis(1-
 oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-
 hydroxy-
 2-(trifluoromethyl)-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

PAGE 1-A

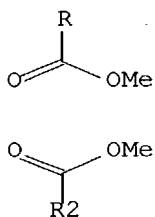
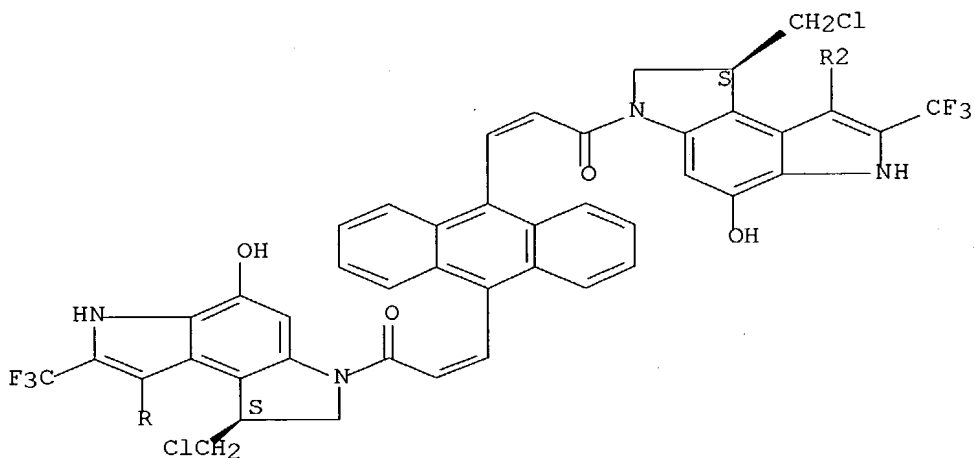


PAGE 1-B



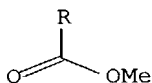
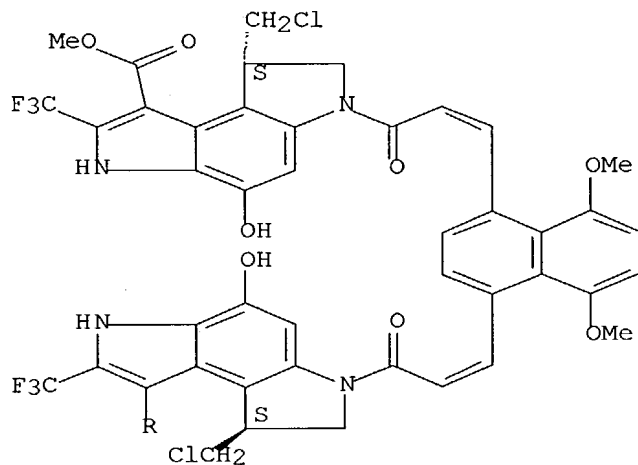
RN 179693-48-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[9,10-
 anthracenediylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



RN 179693-49-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(5,8-dimethoxy-1,4-naphthalenediyl)bis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

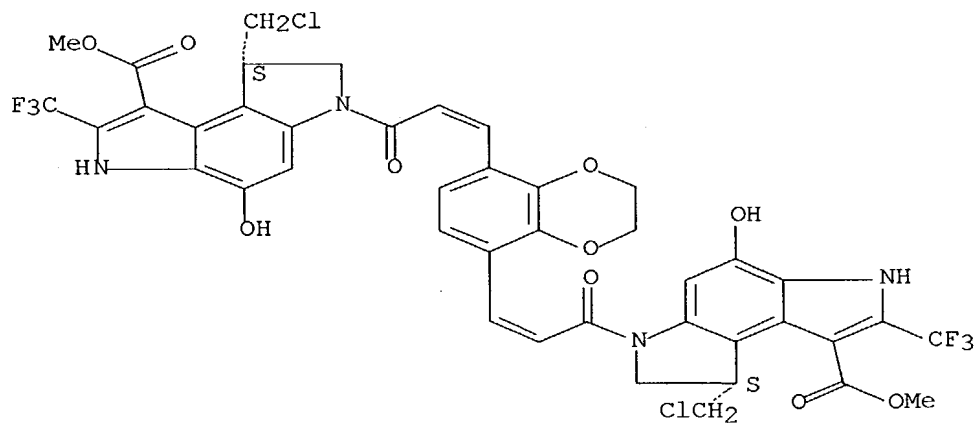


RN 179693-50-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,3-dihydro-1,4-benzodioxin-5,8-diyl)bis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



RN 179693-51-7 CAPLUS

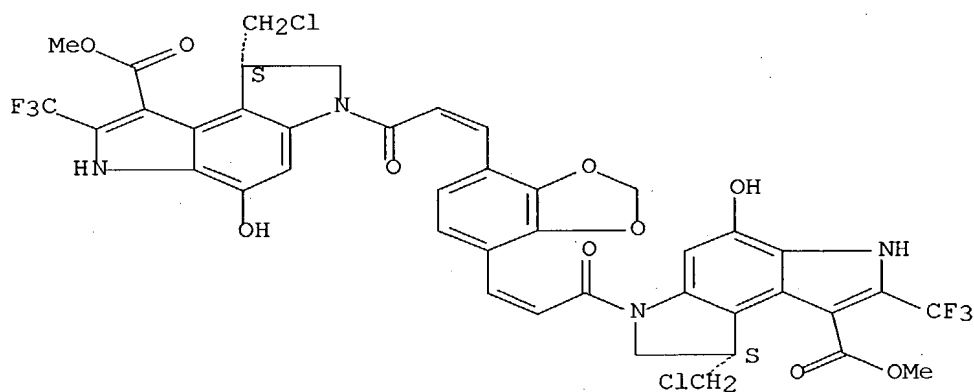
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,3-benzodioxole-4,7-

diylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

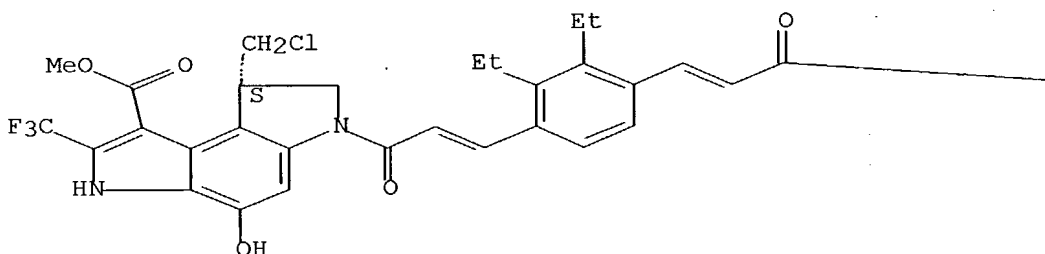


RN 179693-52-8 CAPLUS

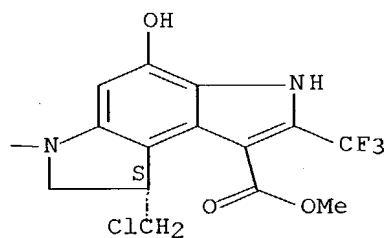
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,3-diethyl-1,4-phenylene)bis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



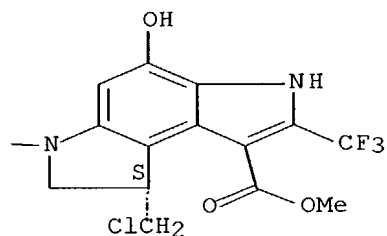
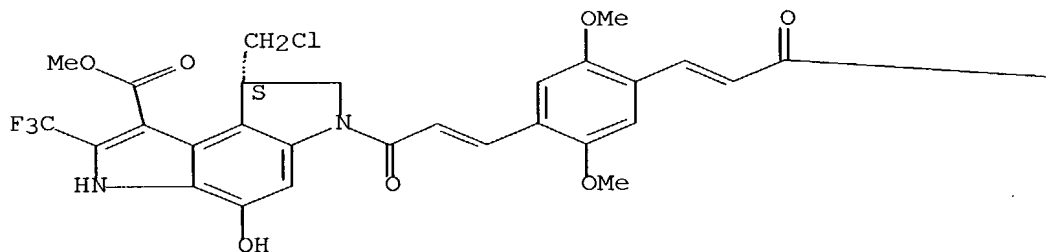
PAGE 1-A



RN 179693-53-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,5-dimethoxy-1,4-phenylene)bis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

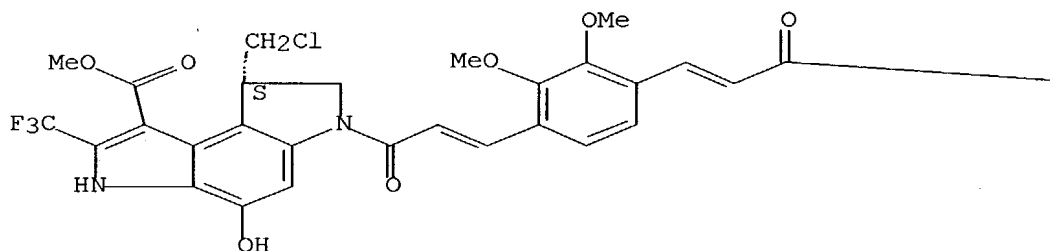


RN 179693-54-0 CAPLUS

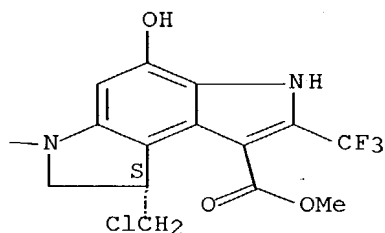
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(2,3-dimethoxy-1,4-phenylene)bis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

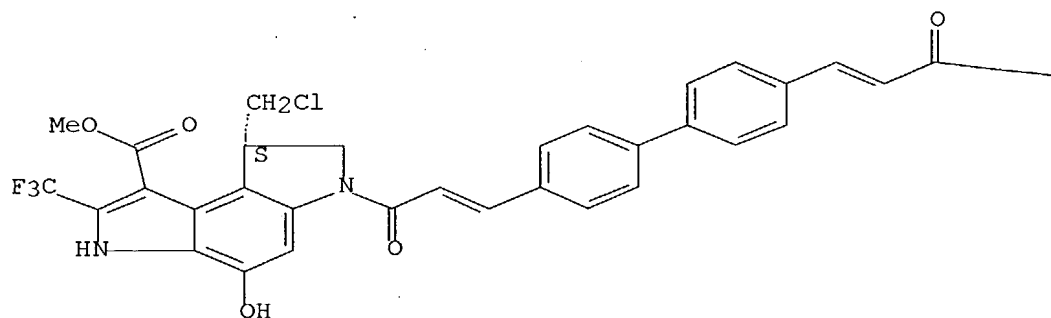


RN 179693-55-1 CAPLUS

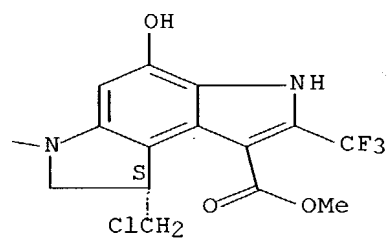
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[1,1'-biphenyl]-4,4'-diylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

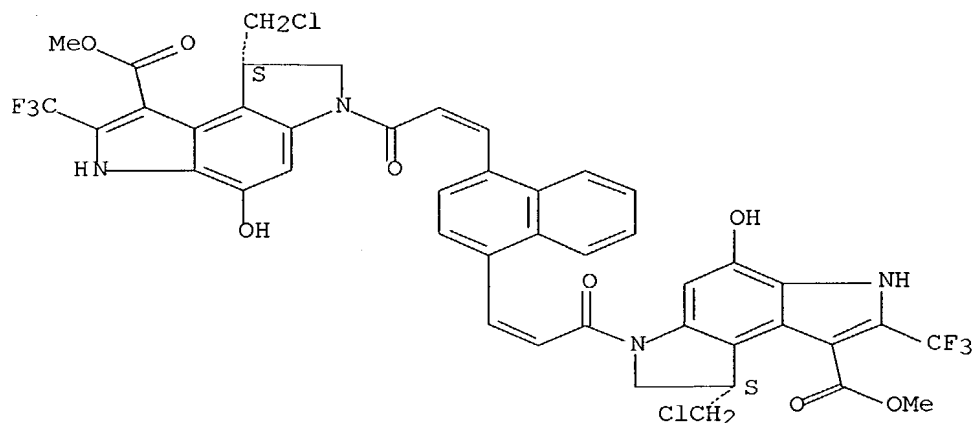


RN 179693-56-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-naphthalenediylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



RN 179693-57-3 CAPLUS

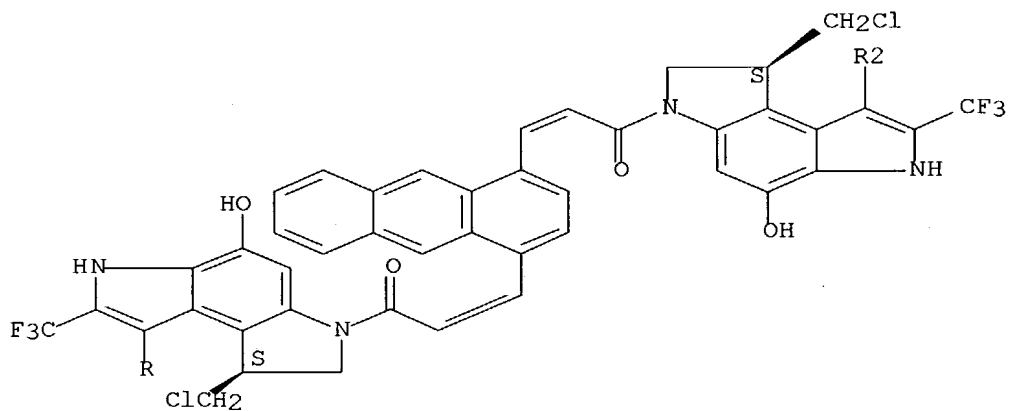
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-anthracenediylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-

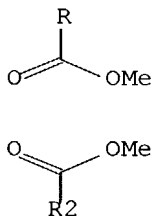
tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

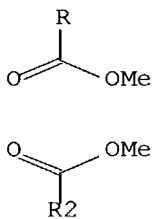
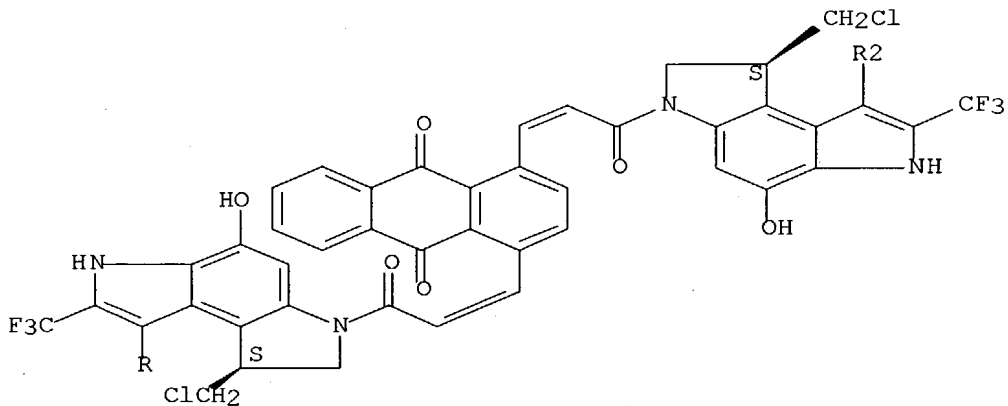
PAGE 1-A





RN 179693-58-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[(9,10-dihydro-9,10-dioxo-1,4-anthracenediyl)bis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

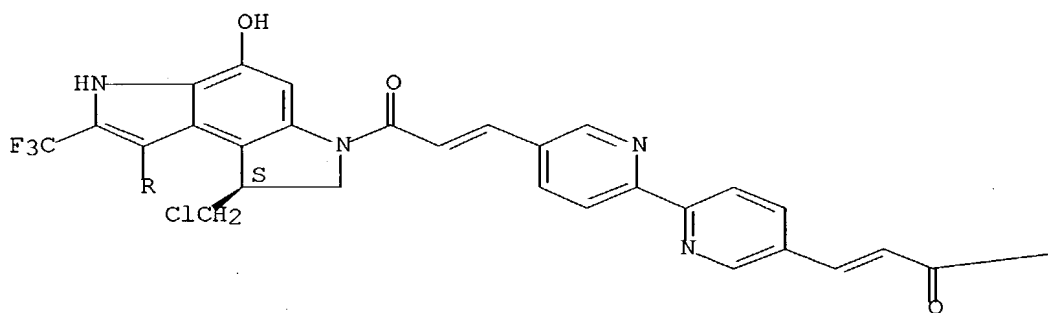
Absolute stereochemistry.
 Double bond geometry unknown.



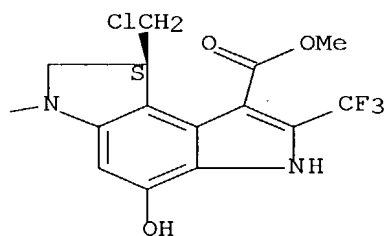
RN 179693-59-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[2,2'-bipyridine]-5,5'-diylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

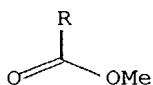
PAGE 1-A



PAGE 1-B



PAGE 2-A

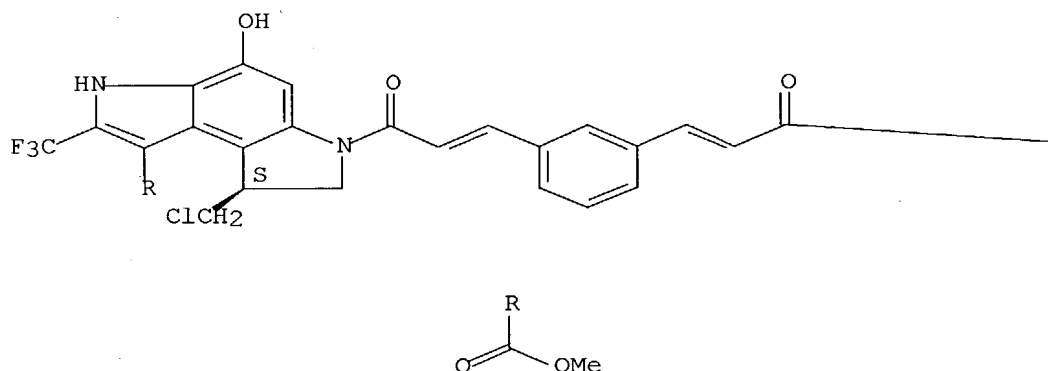


RN 179693-60-8 CAPLUS

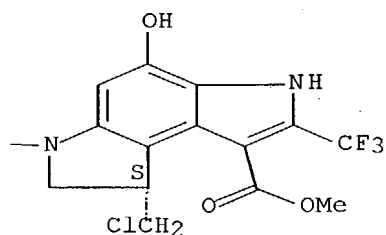
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,3-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



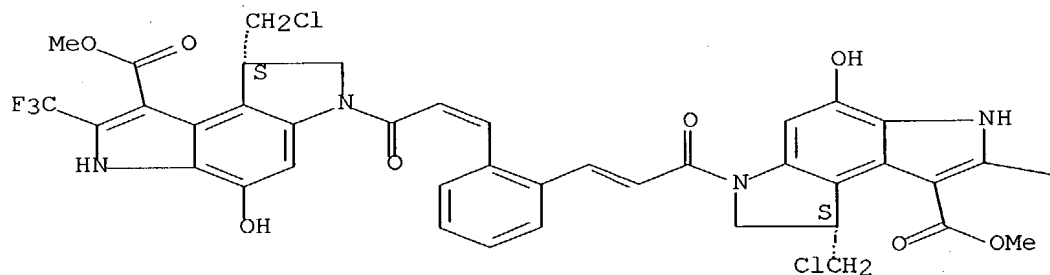
PAGE 1-B



RN 179693-61-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,2-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



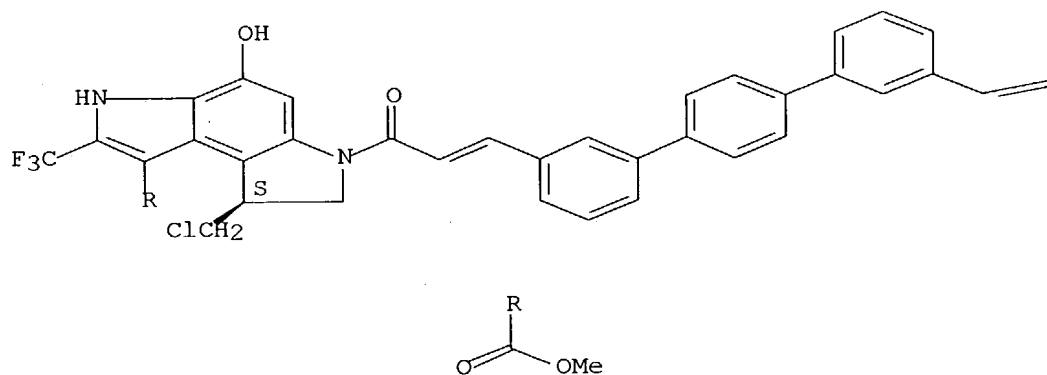
PAGE 1-B

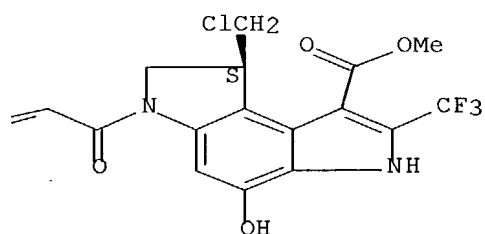
—CF₃

RN 179693-62-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[1,1':4',1''-terphenyl]-3,3''-diylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

PAGE 1-A



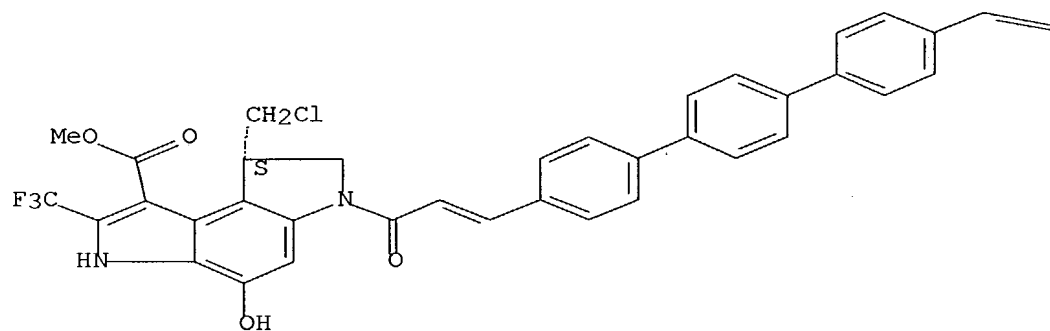


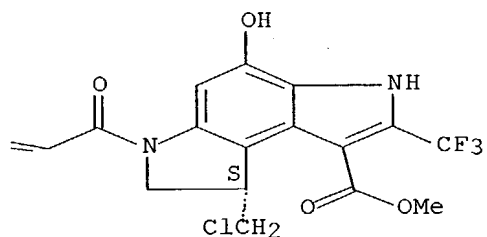
RN 179693-63-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[[1,1':4',1''-terphenyl]-4,4''-diylbis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, dimethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

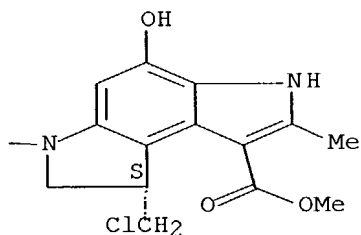
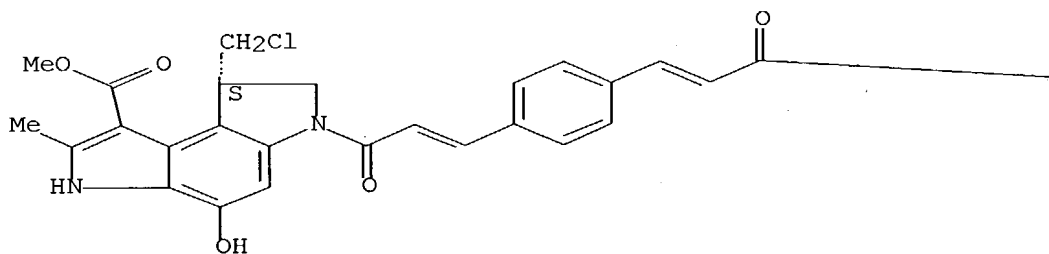
Double bond geometry unknown.





RN 179693-64-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

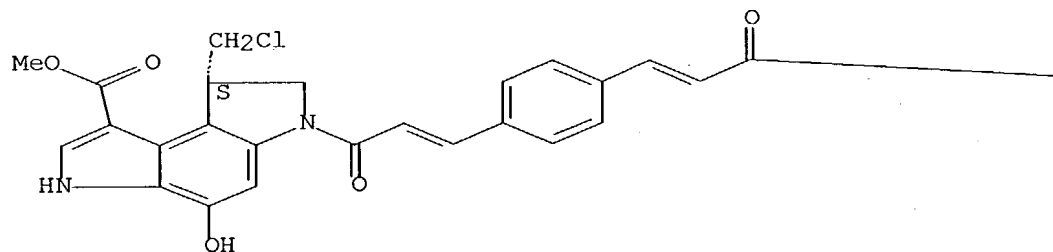


RN 179693-67-5 CAPLUS

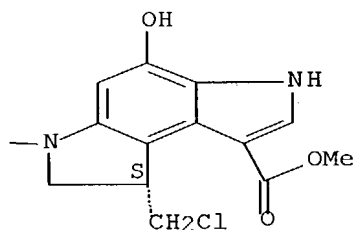
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[1,4-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-
, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



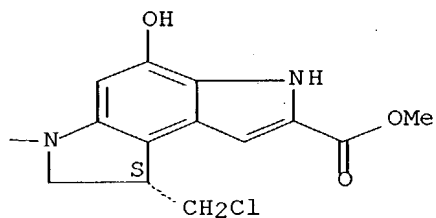
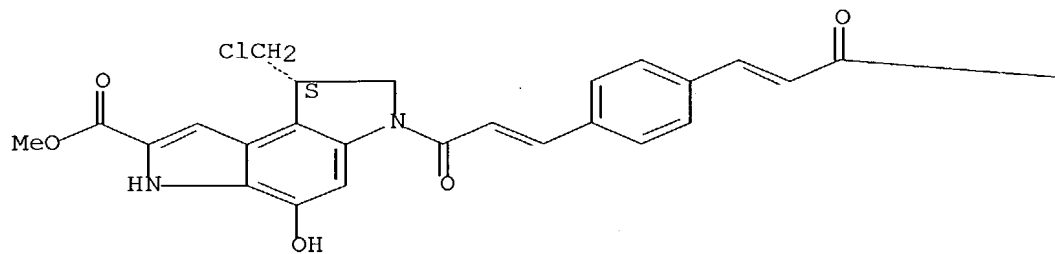
PAGE 1-B



RN 179693-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6,6'-[1,4-phenylenebis(1-oxo-2-propene-3,1-diyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-
, dimethyl ester, (8S,8'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



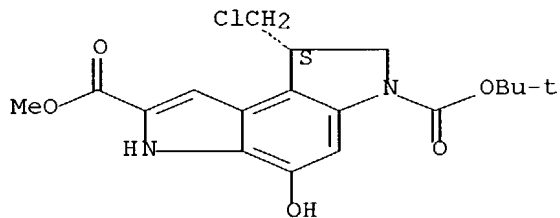
IT 144786-07-2 157904-28-4 176685-42-0
179693-97-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as antitumor agents)

RN 144786-07-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

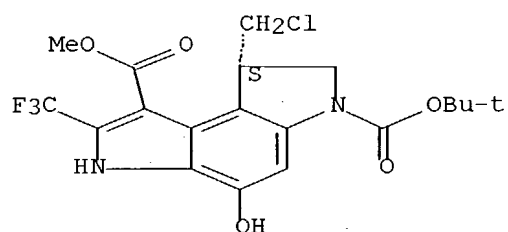


RN 157904-28-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,

6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

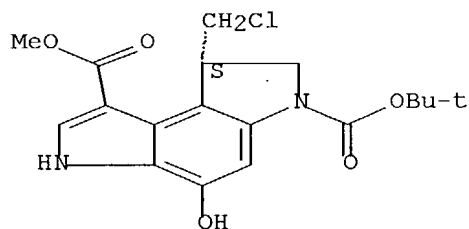
Absolute stereochemistry.



RN 176685-42-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 1-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

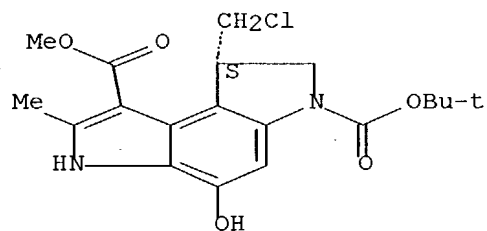
Absolute stereochemistry. Rotation (-).



RN 179693-97-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-methyl-, 6-(1,1-dimethylethyl)
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 68 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:401719 CAPLUS Full-text

DN 125:67752

TI Antitumor agent

IN Saito, Hiromitsu; Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji;

Okamoto, Akihiko; Gomi, Katsushige; Yamashita, Kinya; Sato, Kiyoshi; Nakakura, Masashi; Hayakawa, Eiji

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO PCT Int. Appl., 17 pp.

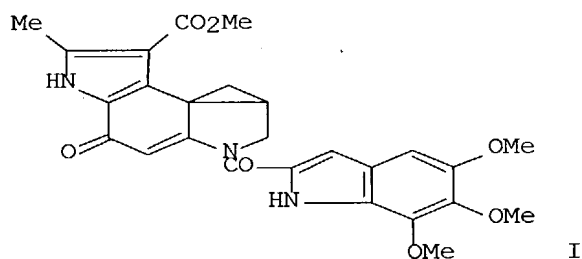
CODEN: PIXXD2

DT Patent

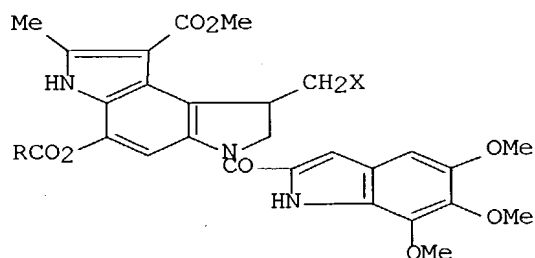
LA Japanese

FAN.CNT 1

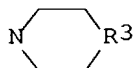
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI.	WO 9610405	A1	19960411	WO 1995-JP1893	19950920
	W:	AU, CA, CN, FI, HU, JP, KR, NO, NZ, US			
	RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
	CA 2201097	AA	19960411	CA 1995-2201097	19950920
	AU 9535328	A1	19960426	AU 1995-35328	19950920
	EP 786252	A1	19970730	EP 1995-932191	19950920
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,			
SE	NO 9701409	A	19970520	NO 1997-1409	19970325
	FI 9701278	A	19970527	FI 1997-1278	19970326
PRAI	JP 1994-237226		19940930		
	WO 1995-JP1893		19950920		
OS	MARPAT 125:67752				
GI					



I



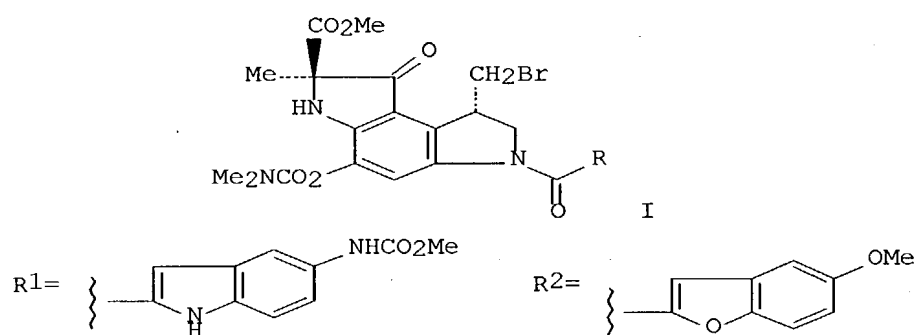
II



III

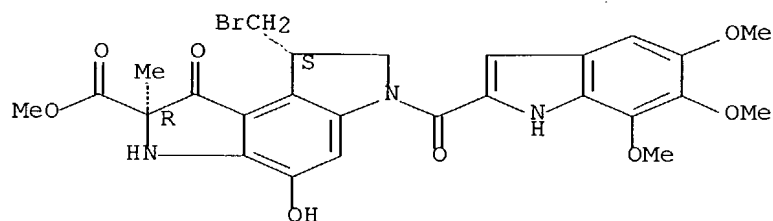
AB An antitumor agent against drug-fast tumors comprises a compound represented by general formula (I) or (II) or a pharmacol. acceptable salt thereof as the active ingredient; wherein X represents Cl or Br; and R represents NR₁R₂ (wherein R₁ and R₂ represent each independently hydrogen or C₁-C₄ linear or branched alkyl) or a group of formula (III) (wherein R₃ represents CH₂ or N-CH₃). The agent has an excellent antitumor activity against drug-insensitive tumors and is useful as an antitumor agent against drug-fast tumors. Capsules were formulated containing I 2, Avecel 117.5, and magnesium stearate 0.5 mg.

L10 ANSWER 69 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:368752 CAPLUS Full-text
 DN 125:114354
 TI Synthesis and antitumor activity of novel duocarmycin derivatives
 AU Asai, Akira; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katushige; Saito, Hiromitsu
 CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co. Ltd., Tokyo, 194, Japan
 SO Bioorganic & Medicinal Chemistry Letters (1996), 6(11), 1215-1220
 CODEN: BMCLE8; ISSN: 0960-894X
 PB Elsevier
 DT Journal
 LA English
 GI



AB A series of Duocarmycin B2 analogs I [R = R1, R2, (E)-CH:CHC6H4OMe-4, (E)-CH:CHC6H4(NHMe)-4, CH2OC6H4OMe-4] bearing simplified right hand segments (Seg-Bs) with the protected phenolic hydroxyl group in left hand segment (Seg-A) was synthesized. Among them, the cinnamoyl derivs. I [R = (E)-CH:CHC6H4OMe-4, (E)-CH:CHC6H4(NHMe)-4] exhibited potent antitumor activity against in vivo murine tumor models in the wider range of doses without detectable toxic effects than DUMB2.
 IT **124325-94-6**, Duocarmycin B2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
 (synthesis and antitumor activity of novel duocarmycin derivs.)
 RN 124325-94-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 171599-25-0P, Duocarmycin B2 N,N-dimethylcarbamate

179239-44-2P 179239-46-4P 179239-48-6P

179239-49-7P 179239-51-1P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological

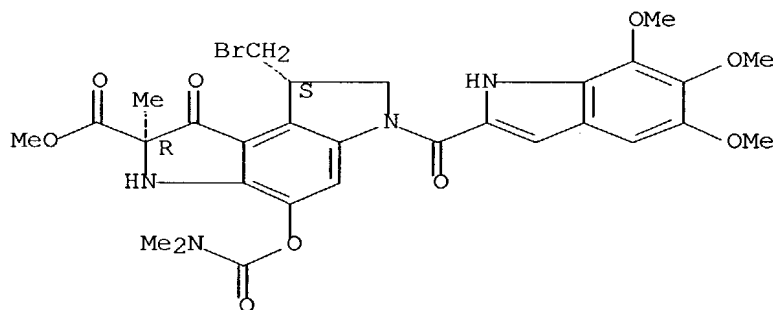
study); PREP (Preparation)

(synthesis and antitumor activity of novel duocarmycin derivs.)

RN 171599-25-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
(9CI) (CA INDEX NAME)

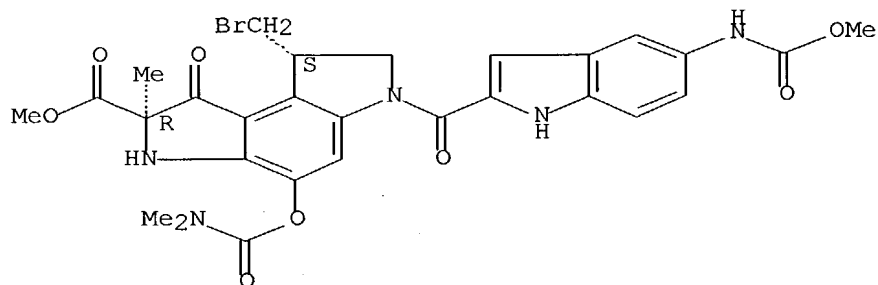
Absolute stereochemistry.



RN 179239-44-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[[5-
[(methoxycarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl
ester, (2R-trans)- (9CI) (CA INDEX NAME)

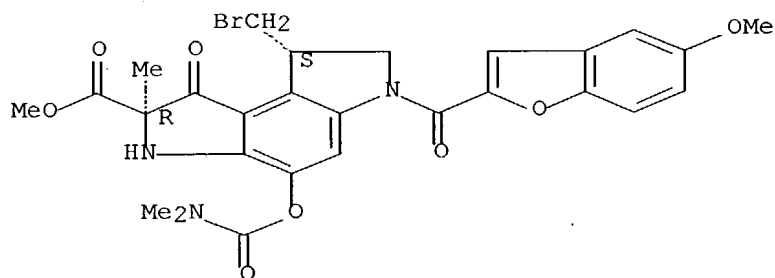
Absolute stereochemistry.



RN 179239-46-4 CAPLUS

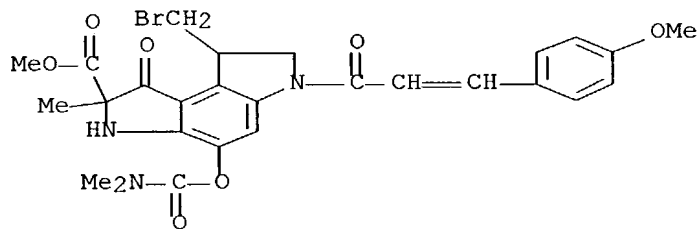
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(5-methoxy-2-benzofuranyl) carbonyl]-2-methyl-1-oxo-, methyl ester, (2R-trans)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 179239-48-6 CAPLUS

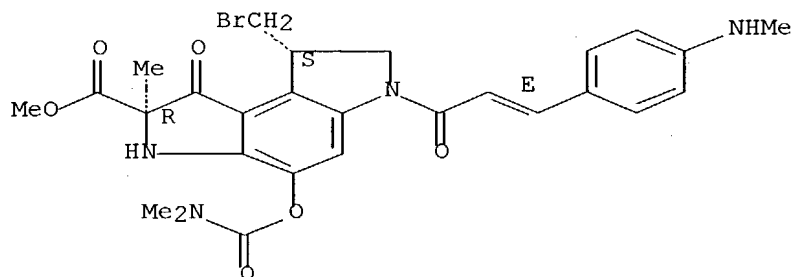
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester, [2R-[2α,6(E),8β]]- (9CI) (CA INDEX NAME)



RN 179239-49-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[3-[4-
(methylamino)phenyl]-1-oxo-2-propenyl]-1-oxo-, methyl ester,
[2R-[2 α ,6(E),8 β]]- (9CI) (CA INDEX NAME)

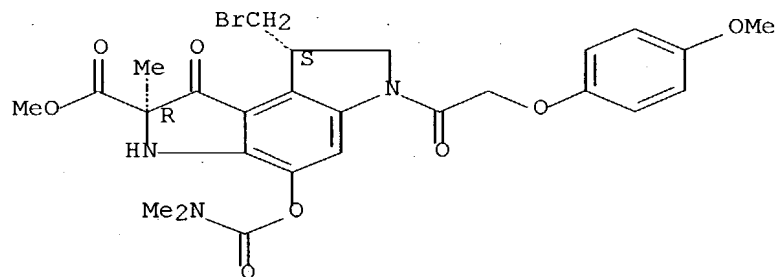
Absolute stereochemistry.
Double bond geometry as shown.



RN 179239-51-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(4-
methoxyphenoxy)acetyl]-2-methyl-1-oxo-, methyl ester, (2R-trans)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT 179108-37-3P 179239-43-1P 179239-45-3P
179239-47-5P 179239-50-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

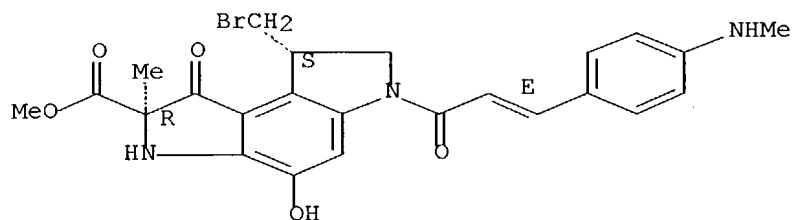
(synthesis and antitumor activity of novel duocarmycin derivs.)

RN 179108-37-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-6-[3-[4-(methylamino)phenyl]-1-
oxo-2-propenyl]-1-oxo-, methyl ester, [2R-[2 α ,6(E),8 β]]- (9CI)
(CA INDEX NAME)

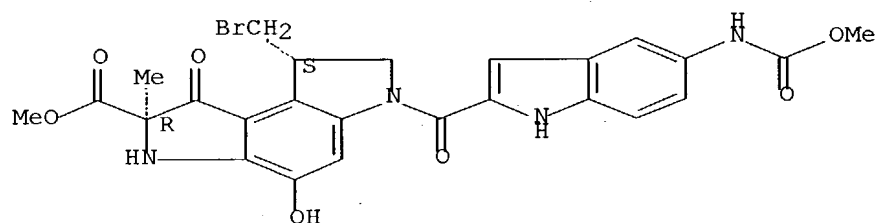
Absolute stereochemistry.

Double bond geometry as shown.



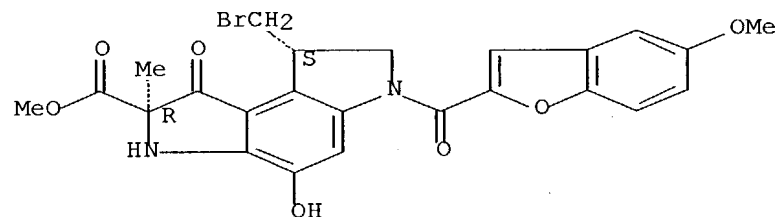
RN 179239-43-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-6-[[5-[(methoxycarbonyl)amino]-1H-indol-
 2-yl]carbonyl]-2-methyl-1-oxo-, methyl ester, (2R-trans)- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.



RN 179239-45-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-6-[(5-methoxy-2-benzofuranyl)carbonyl]-
 2-methyl-1-oxo-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



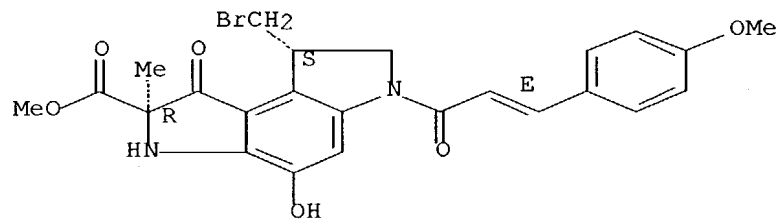
RN 179239-47-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-

propenyl]-2-

methyl-1-oxo-, methyl ester, [2R-[2 α ,6(E),8 β]]- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

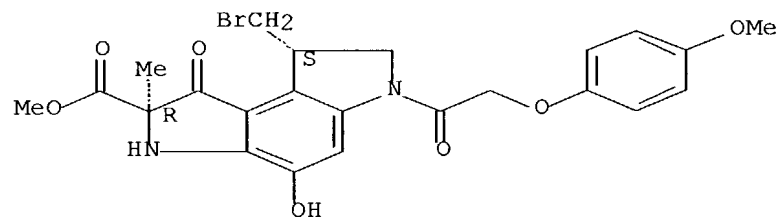
Double bond geometry as shown.



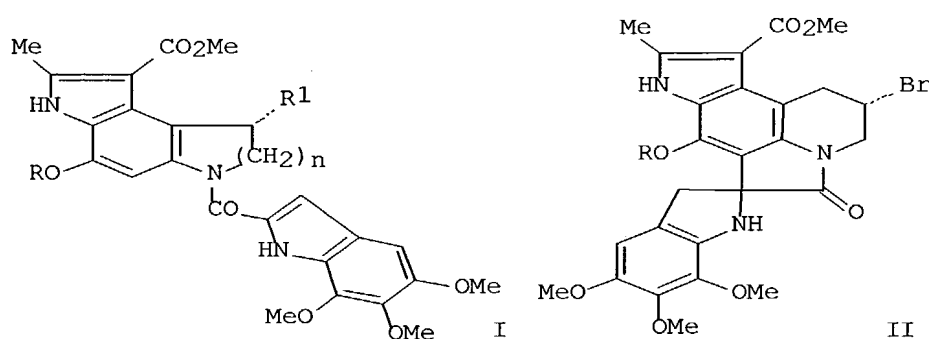
RN 179239-50-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-6-[(4-methoxyphenoxy)acetyl]-2-methyl-1-
oxo-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 70 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:325161 CAPLUS Full-text
 DN 125:58167
 TI Wagner-Meerwein rearrangement of duocarmycins
 AU Nagamura, Satoru; Kanada, Yutaka; Asai, Akira; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
 CS Tokyo Research Laboratories, Kyowa Hakko Kogyo co., Ltd., Machida, 194, Japan
 SO Chemical & Pharmaceutical Bulletin (1996), 44(5), 933-939
 CODEN: CPBTAL; ISSN: 0009-2363
 PB Pharmaceutical Society of Japan
 DT Journal
 LA English
 GI



AB Treatment of 8-O-protected-3-hydroxy derivs. of duocarmycin B2 with camphorsulfonic acid (CSA) in toluene interestingly gave A-ring pyrrole analogs I [R = SiMe₂CMe₃, CONMe₂, 4-methylpiperazinecarbonyl (Q), R₁ = CH₂Br, n = 1]. Their structures were unambiguously elucidated on the basis of NMR and mass spectrometry, and the mechanism was considered to be a Wagner-Meerwein type rearrangement. On the other hand, treatment of 9-O-protected-3-hydroxy derivs. of duocarmycin B1 with CSA afforded different rearrangement products. In the case of bulky groups at the 9-O position, such as a tert-butyldimethylsilyl group, the normal A-ring pyrrole analog I [R = SiMe₂CMe₃, R₁ = Br, n = 2] was obtained. Under the same conditions, however, the 9-O-N,N-dimethylcarbamoyl-3-hydroxy compound gave the spiro compound II [R = CONMe₂], which was derived from a 1,2-shift of the methoxycarbonyl group and a bonding between the C-8 position and the C-2' position. The Q-protected compound gave a mixture of I [R = Q, R₁ = Br, n = 2] and II [R = Q]. I have antitumor activity, whereas II do not.

IT 154889-68-6P 177958-19-9P 177958-20-2P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(Wagner-Meerwein rearrangement of duocarmycins)

RN 154889-68-6 CAPLUS

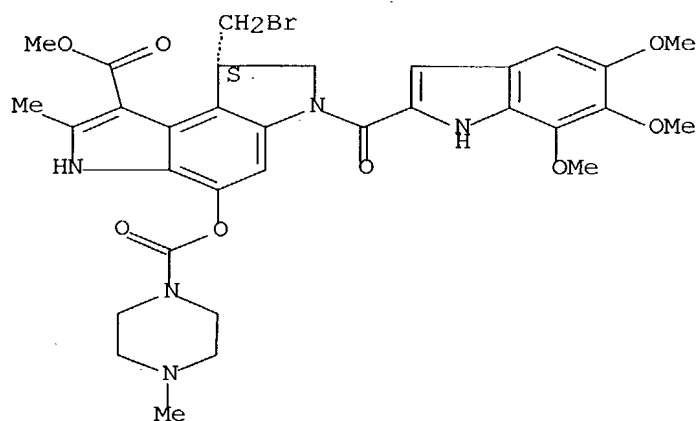
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



RN 177958-19-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

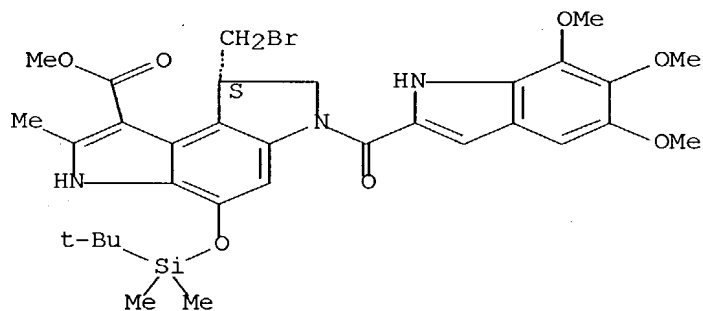
[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



RN 177958-20-2 CAPLUS

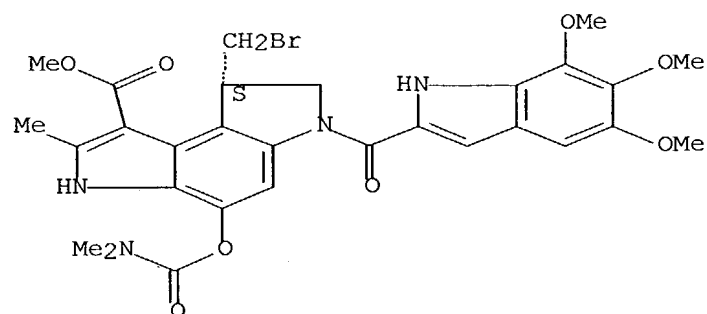
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(dimethylamino) carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



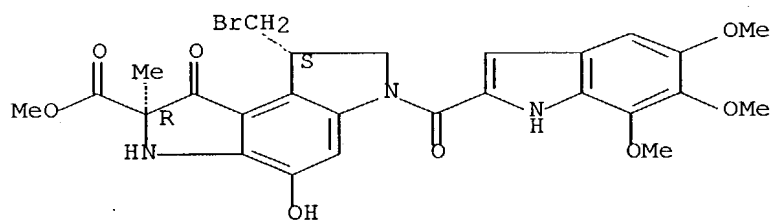
IT 124325-94-6, Duocarmycin B2 154901-65-2
171599-25-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(Wagner-Meerwein rearrangement of duocarmycins)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

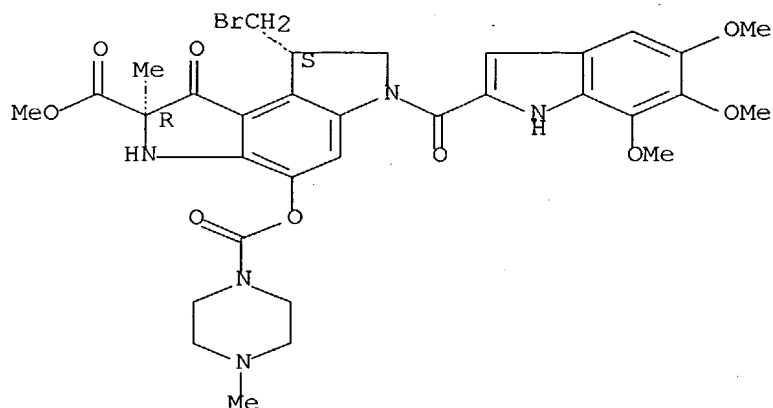
Absolute stereochemistry.



RN 154901-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-
piperazinyl)carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(2R,8S)-
(9CI) (CA INDEX NAME)

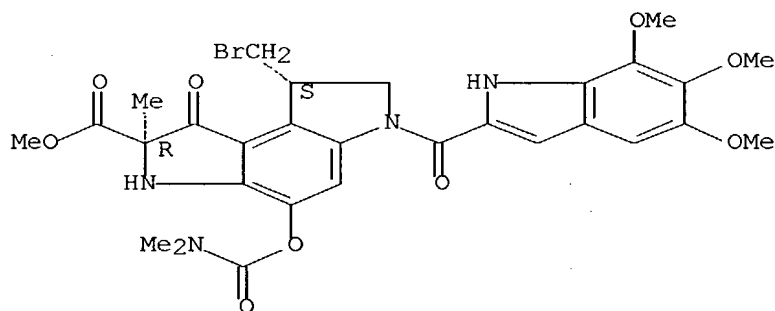
Absolute stereochemistry.



RN 171599-25-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 129953-15-7P 129953-17-9P 160819-29-4P
 177958-18-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

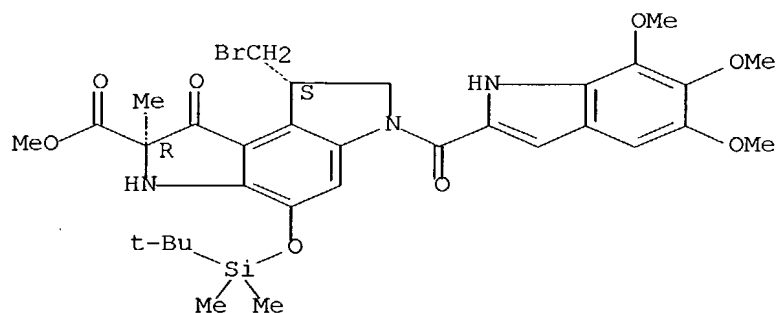
(Reactant or reagent)

(Wagner-Meerwein rearrangement of duocarmycins)

RN 129953-15-7 CAPLUS

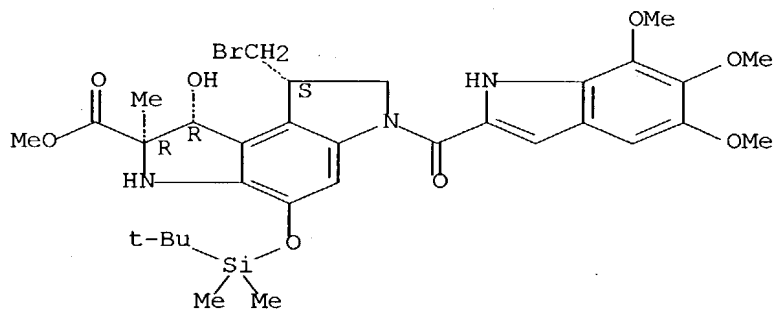
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-
 (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



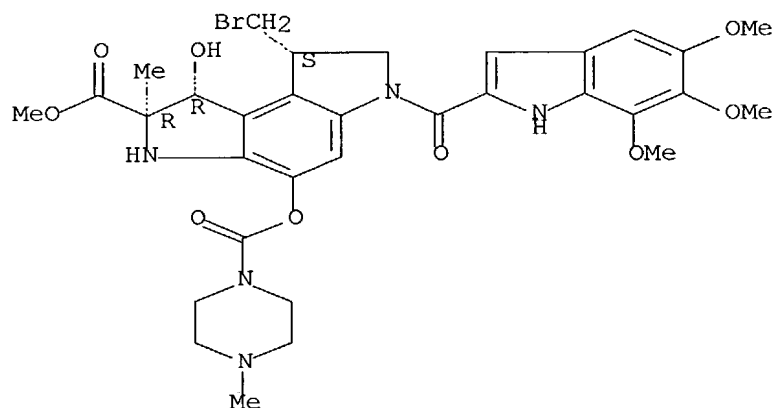
RN 129953-17-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-
 6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



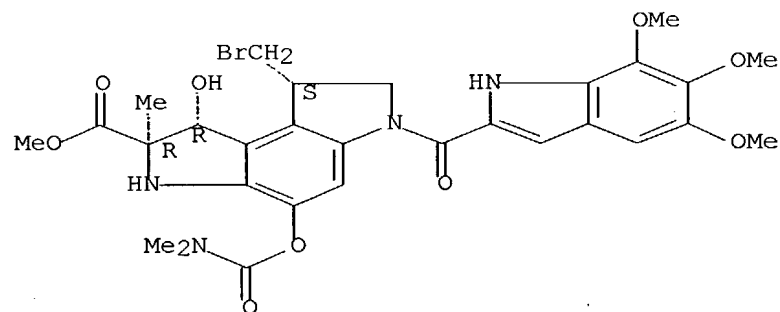
RN 160819-29-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



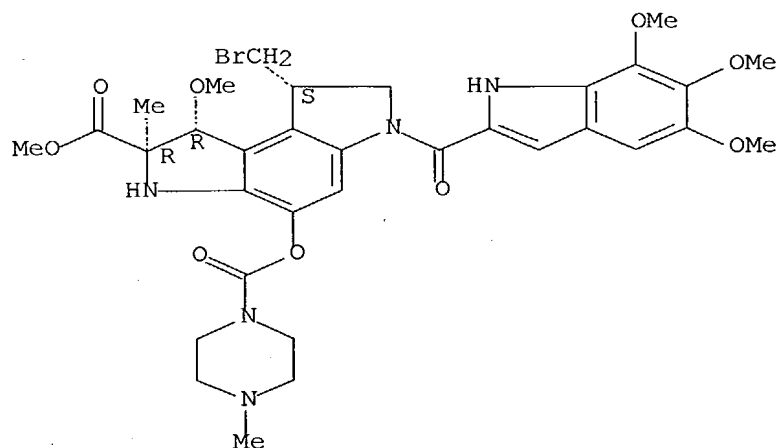
RN 177958-18-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-
 6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
 [1R-(1 α ,2 β ,8 α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 177958-21-3P 178036-26-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (Wagner-Meerwein rearrangement of duocarmycins)
 RN 177958-21-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-4-[[(4-methyl-1-
 piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl ester, [1R-(1 α ,2 β ,8 α)]- (9CI) (CA INDEX NAME)

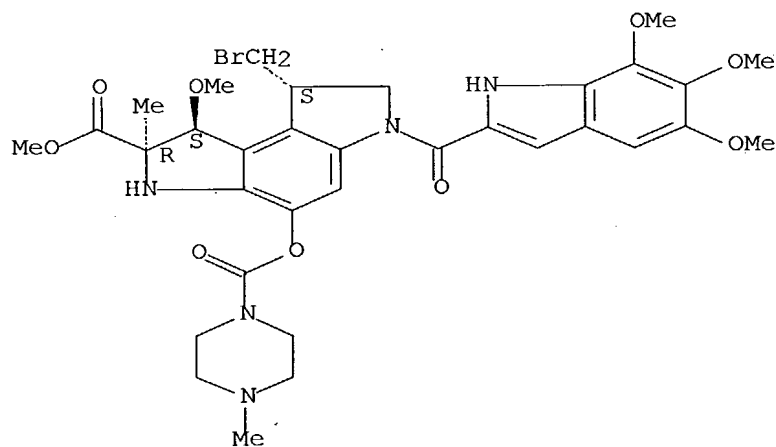
Absolute stereochemistry.



RN 178036-26-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-4-[[(4-methyl-1-
 piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-,
 methyl ester, [1S-(1 α ,2 α ,8 β)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 71 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:303718 CAPLUS Full-text
 DN 124:343269
 TI Preparation of pyrroloindole derivatives as antitumor agents
 IN Terajima, Atsuro; Fukuda, Yasumichi; Furuta, Kosuke; Oomori, Yasuo; Ko, Hiroyuki
 PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
 SO Jpn. Kokai Tokkyo Koho, 16 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	JP 08034789	A2	19960206	JP 1994-174475	19940726
PRAI	JP 1994-174475		19940726		
OS	MARPAT 124:343269				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I and II; R = C1-4 lower alkyl; R1 = α -amino acid residue, Q, Q1, Q3, Q4, Q5, Q6, CO-W-CO; R2 = H, HO-protective group, group degradable in vivo; Y = halo, arylsulfonyloxy, lower alkanesulfonyloxy, haloalkanesulfonyloxy, N3; wherein X1, X2, X3 = H, OH, OR3, O2CR3, CHO, NO2, NR4R5, NR4COR5, NR4CO2R3, Q2, CH2NR4R5, NHCOR4R5; X4, X5, X6 = H, OR3; X7, X13 = O, S, NH; X8, X9, X10, X11, X12, X14 = CH, N; n = 0-2; wherein R3 = (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; R4, R5 = H, (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; W = (CH2)m, (CH2)m-Z4-(CH2)n, Q7; wherein m, n = 0-16; Z4 = S, O, NH], optical isomers, and pharmacol. acceptable salts, which show highly selective anticancer activity and low toxicity, are effective against solid tumors, and also have antibacterial activity, are prepared Thus, 20 mg pyrrolo[3,2-e]indole derivative I (R = Me, R1 = Boc, R2 = H, Y = Cl) (preparation given) was treated with 3 M HCl/EtOAc, stirred for 1 h, and after distilling off the solvent, stirred with 13.2 mg 5,6,7-trimethoxy-1H-indole-2-carboxylic acid and 30.2 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in DMF at room temperature overnight to give 79% I (R = Me, R1 = Q8, R2 = H, Y = Cl). The latter compound (10.6 mg) was suspended in MeCN, treated with 6.2 μ L 1,8-diazabicyclo[5.4.0]-7-undecene, and stirred at room temperature for 5 h to give the title compound cyclopropa[c]pyrrolo[3,2-e]indole (7bR,8aS)-II (R = Me, R1 = Q8). The title compound I (R = Me, R1 = Q9, R2 = H, Y = Cl) in vitro showed IC50 of 0.048 ng/mL against HeLa S3 cells and at 0.25 mg/kg in vivo inhibited by 69% the growth of colon 26 cancer cells in mice.

IT 176685-39-5P 176685-40-8P 176685-41-9P
 176685-42-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

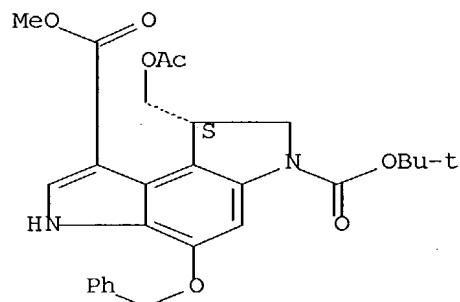
(Reactant or reagent)

(preparation of pyrrolobenzocarbazole and
 cyclopropapyrrolobenzocarbazole
 letrione derivs. as antitumor agents)

RN 176685-39-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-
dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

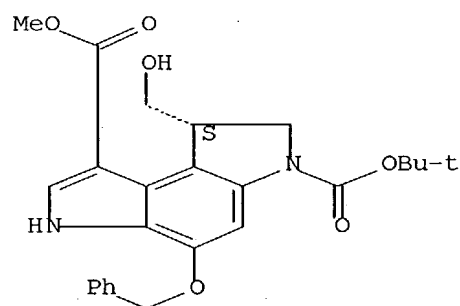
Absolute stereochemistry. Rotation (-).



RN 176685-40-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

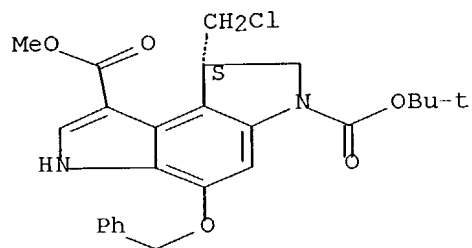
Absolute stereochemistry. Rotation (-).



RN 176685-41-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

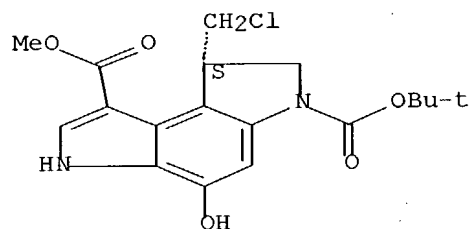
Absolute stereochemistry. Rotation (-).



RN 176685-42-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 1-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



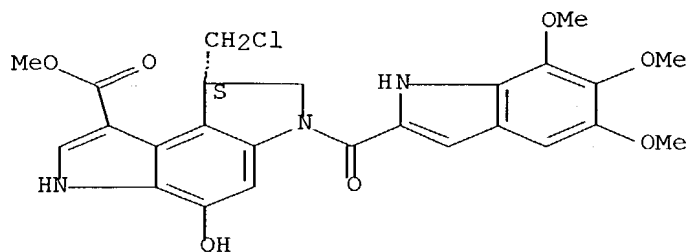
IT 176685-35-1P 176685-36-2P 176685-37-3P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrroloindole and cyclopropapyrroloindole derivs. as
antitumor agents)

RN 176685-35-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
methyl
ester, (8S)- (9CI) (CA INDEX NAME)

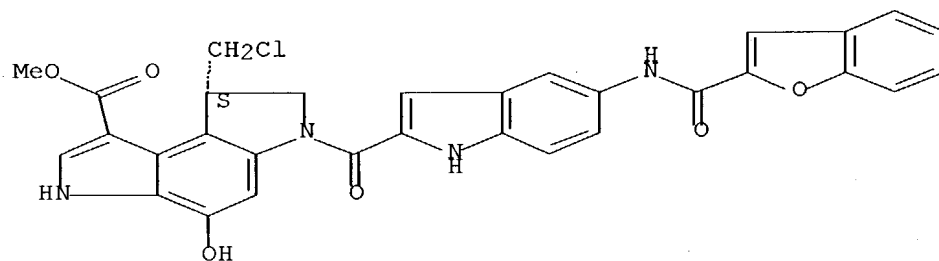
Absolute stereochemistry. Rotation (-).



RN 176685-36-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

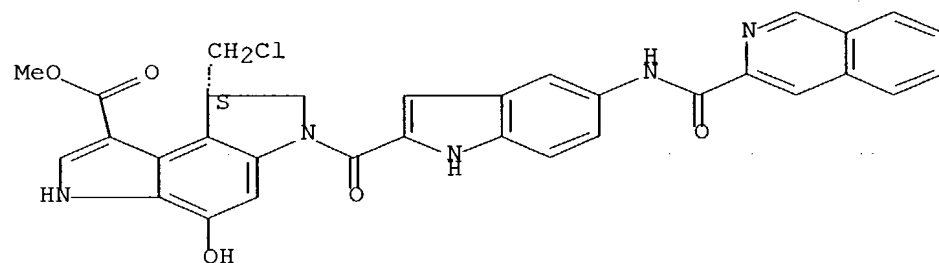
Absolute stereochemistry. Rotation (+).



RN 176685-37-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L10 ANSWER 72 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:115202 CAPLUS Full-text

DN 124:156002

TI Method for stabilizing duocarmycin derivatives

IN Nakakura, Masashi; Ueno, Yuji; Hayakawa, Eiji; Kuroda, Tokuyuki

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO PCT Int. Appl., 16 pp.

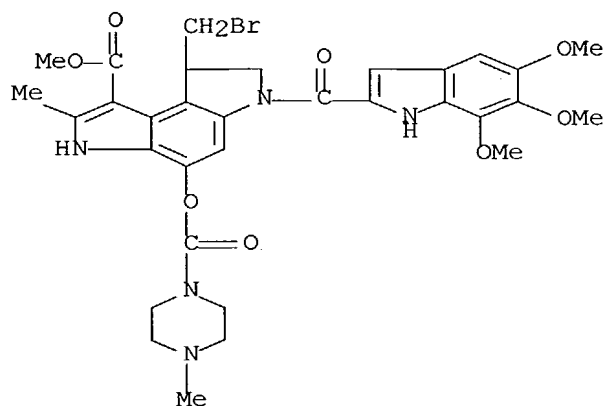
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

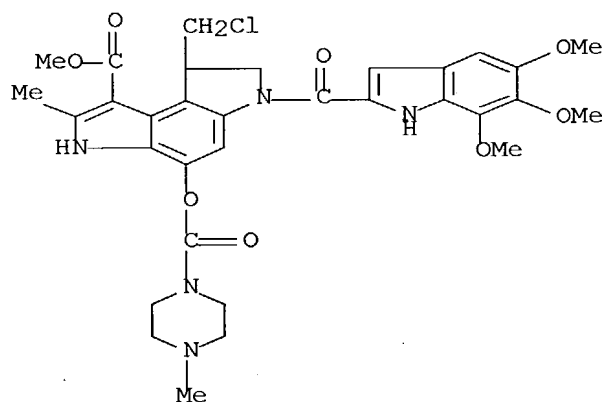
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 9531971	A1	19951130	WO 1995-JP962	19950519
	W: AU, BR, CA, CN, CZ, FI, HU, KR, MX, NO, NZ, PL, RO, RU, SI, SK,				
US	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	JP 07309761	A2	19951128	JP 1994-106415	19940520
	AU 9524551	A1	19951218	AU 1995-24551	19950519
	EP 754030	A1	19970122	EP 1995-918749	19950519
	EP 754030	B1	20001220		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,				
SE	CN 1148805	A	19970430	CN 1995-193164	19950519
	BR 9507640	A	19970819	BR 1995-7640	19950519
	HU 78072	A2	19990830	HU 1996-3521	19950519
	AT 198149	E	20010115	AT 1995-918749	19950519
	US 5703080	A	19971230	US 1996-737145	19961030
	NO 9604813	A	19961113	NO 1996-4813	19961113
	FI 9604624	A	19961119	FI 1996-4624	19961119
PRAI	JP 1994-106415	A	19940520		
	WO 1995-JP962	W	19950519		
OS	MARPAT 124:156002				
AB	Stabilized duocarmycin derivs. are prepared by adding at least a compound selected from the group consisting of saccharides, electrolytes, water-soluble polymers, polyhydric alcs. and surfactants to a solution containing the duocarmycin derivs. Also provided are freeze-dried pharmaceutical prepns. containing the stabilized duocarmycin derivs. Citric acid 50, duocarmycin·HBr (I) 100, and lactose 5000 mg were dissolved in distilled water to make a total volume of 200 mL. The resulting solution was placed into vials in 2 mL portions, and freeze-dried under reduced pressure. After storage at 60° for 30 days, HPLC anal. showed that 100% of I remained.				
IT	134106-78-8 134106-81-3 173552-35-7				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (freeze-dried prepns. containing stabilized duocarmycin derivs.)				
RN	134106-78-8 CAPLUS				
CN	Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)				



RN 134106-81-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

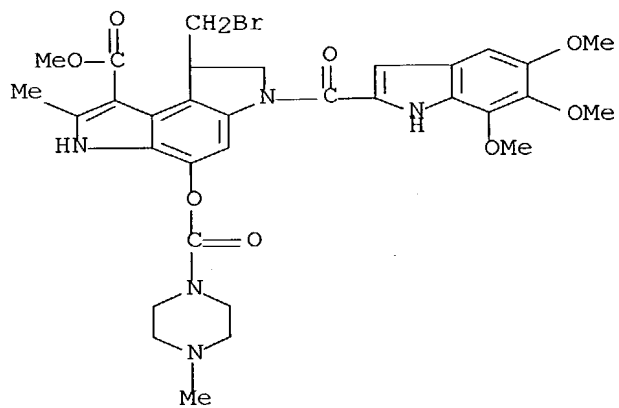
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 173552-35-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

PAGE 1-A



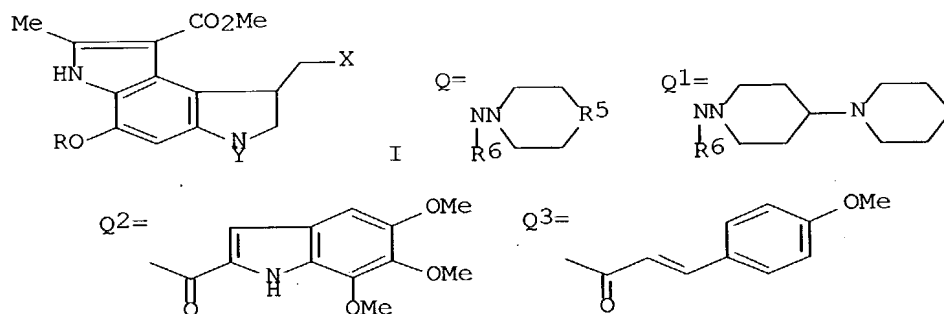
● HBr

PAGE 2-A

● H₂O

L10 ANSWER 73 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:998395 CAPLUS Full-text
 DN 124:176153
 TI Preparation of DC-89 derivatives as antitumor agents
 IN Amishiro, Nobuyoshi; Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji; Okamoto, Akihiko; Gomi, Katsushige
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9529179	A1	19951102	WO 1995-JP779	19950420
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2165819	AA	19951102	CA 1995-2165819	19950420
	AU 9522671	A1	19951116	AU 1995-22671	19950420
	AU 685939	B2	19980129		
	EP 705833	A1	19960410	EP 1995-916020	19950420
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5641780	A	19970624	US 1995-564178	19951215
PRAI	JP 1994-84714	A	19940422		
	WO 1995-JP779	W	19950420		
OS	MARPAT 124:176153				
GI					



AB DC-89 derivs. [I; X = Cl or Br; R = (un)substituted alkyl, (un)substituted aralkyl, COR1, OR2, SR2, NR3R4, Q, Q1, SO2R8; wherein R1 = H, (un)substituted alkyl, aryl, or heterocyclyl; R2 = (un)substituted alkyl, aryl; R3, R4 = H, (un)substituted alkyl, NH2, mono- or dialkylamino; provided that R3 = R4 ≠ H; R5 = NR7, O; R6, R7 = H, (un)substituted alkyl; R8 = (un)substituted alkyl or aryl; Y = Q2, Q3] or pharmacol. acceptable salts thereof are prepared. Thus, the tert-butyltrimethylsilyl ether I (R = Me₃CSiMe₂, X = Br, Y = Q2) (50 mg) was dissolved in THF, treated with 0.11 mL 1.0 M Bu₄NF/THF, and stirred at room temperature for 1 h to give, after workup, the alc. I (R = H, X = Br, Y = Q2) which was dissolved in MeCN, treated with 48% aqueous HBr, stirred at room temperature for 1 h, treated with 1 N aqueous HBr, and extracted with CHCl₃. The CHCl₃ extract was dried over anhydrous Na₂SO₄ and evaporated to dryness to give the crude product which was dissolved in CH₂Cl₂, treated with 0.027 mL Ph chloroformate and 0.030 mL Et₃N, and stirred at -78° to 0° for 1 h to give, after workup and silica gel chromatog., the title pyrroloindoline I (R = CO₂Ph, X = Br, Y = Q2).

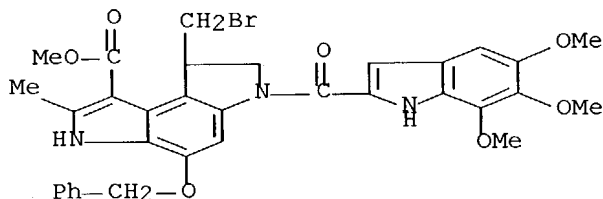
The latter compound in vitro showed IC₅₀ of 0.051 nM for inhibiting the proliferation of HeLaS3 cells and in vivo exhibited T/C of 0.090 (tumor volume of the treated animal/tumor volume of the control) in mice transplanted with sarcoma 180.

IT 173903-48-5P 173903-49-6P 173903-50-9P
 173903-51-0P 173903-52-1P 173903-53-2P
 173903-54-3P 173903-55-4P 173903-56-5P
 173903-57-6P 173903-58-7P 173903-59-8P
 173903-60-1P 173903-61-2P 173903-62-3P
 173903-63-4P 173903-64-5P 173903-65-6P
 173903-66-7P 173903-67-8P 173903-68-9P
 173903-69-0P 173903-70-3P 173903-71-4P
 173903-72-5P 173903-73-6P 173903-74-7P
 173903-75-8P 173903-76-9P 173903-77-0P
 173903-78-1P 173903-79-2P 173903-80-5P
 173903-81-6P 173903-82-7P 173903-83-8P
 173903-84-9P 173903-85-0P 173903-86-1P
 173903-87-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of DC-89 (pyrroloindoline) derivs. as antitumor agents)

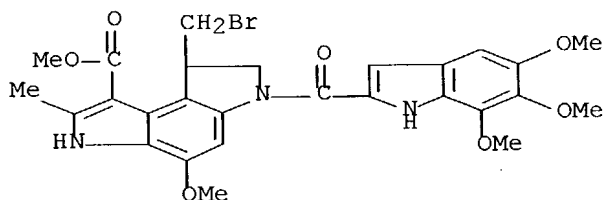
RN 173903-48-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



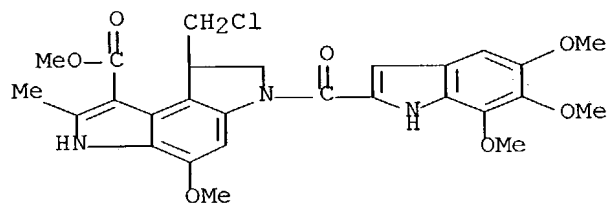
RN 173903-49-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



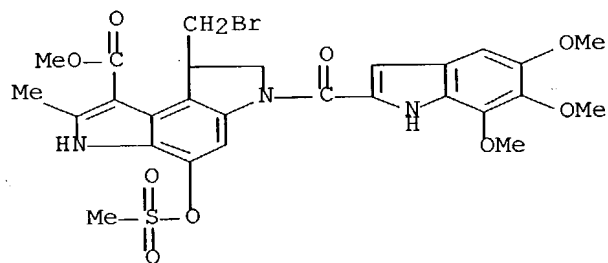
RN 173903-50-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



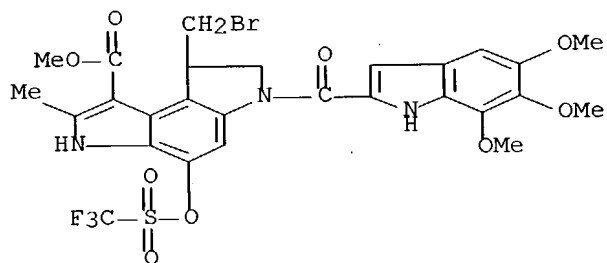
RN 173903-51-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(methylsulfonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



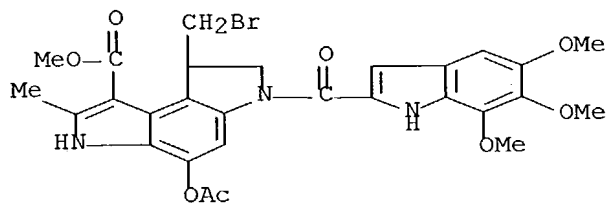
RN 173903-52-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(trifluoromethyl)sulfonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



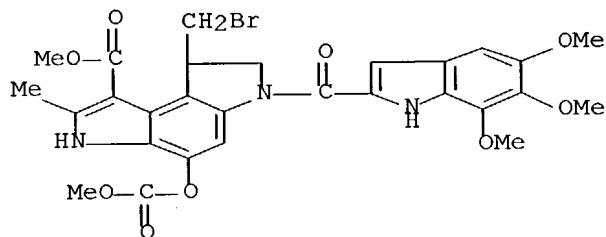
RN 173903-53-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



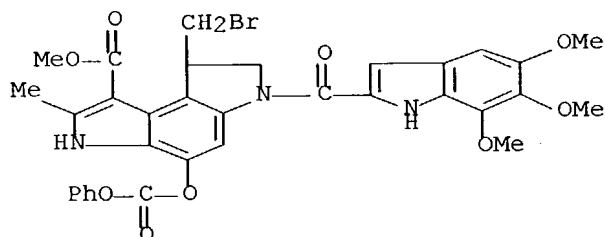
RN 173903-54-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



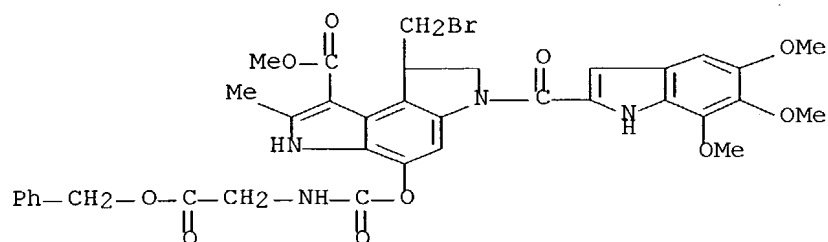
RN 173903-55-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(phenoxy)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



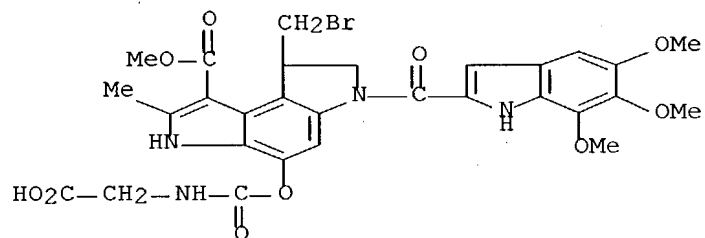
RN 173903-56-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



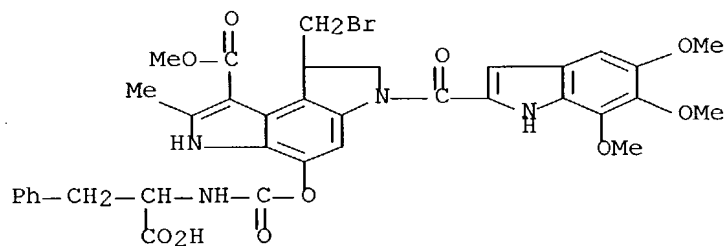
RN 173903-57-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)



RN 173903-58-7 CAPLUS

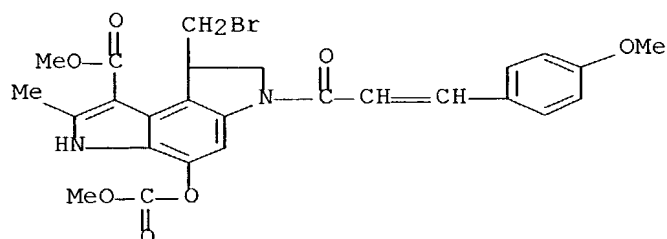
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1-carboxy-2-phenylethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)



RN 173903-59-8 CAPLUS

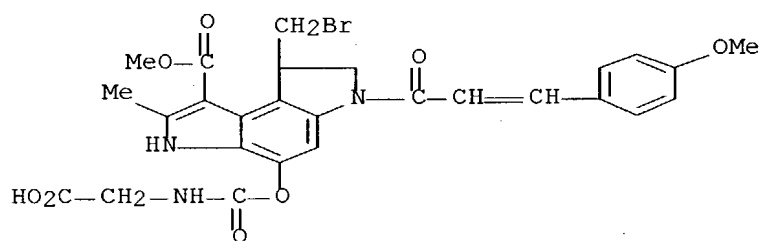
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(4-methoxyphenyl)-1-oxo-2-

propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



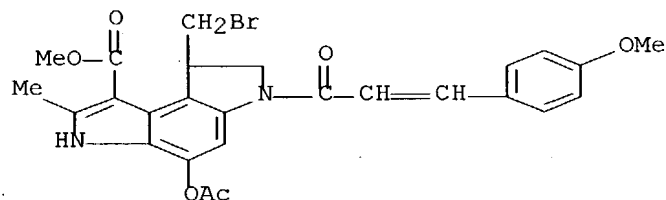
RN 173903-60-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester (9CI) (CA INDEX NAME)



RN 173903-61-2 CAPLUS

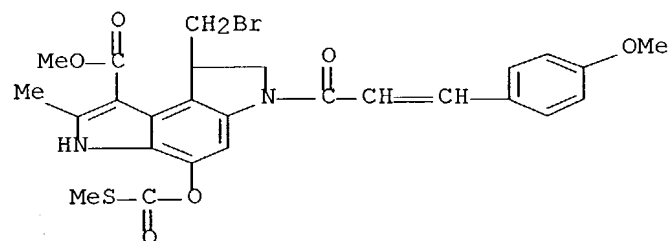
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-62-3 CAPLUS

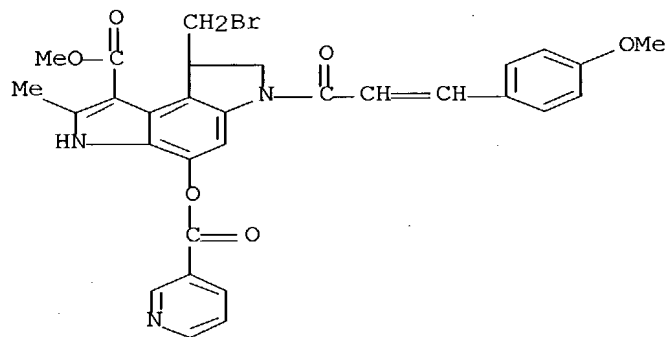
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-

[[(methylthio)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-63-4 CAPLUS

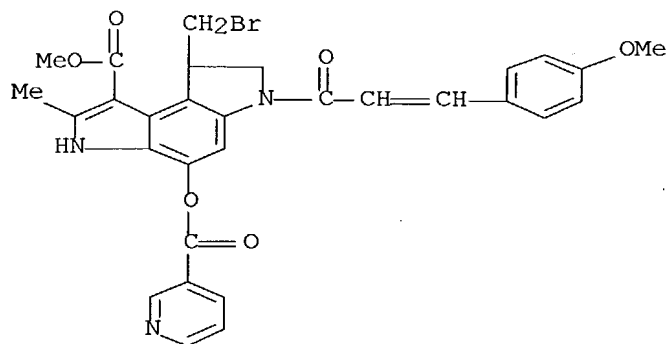
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-64-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, monohydrochloride (9CI) (CA

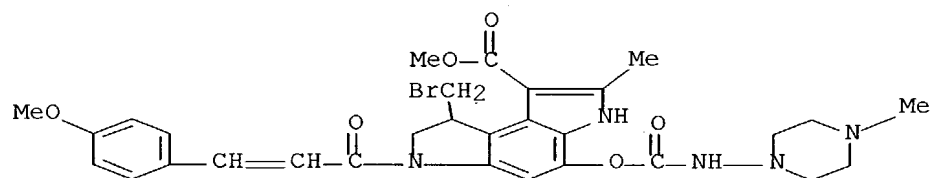
INDEX
NAME)



● HCl

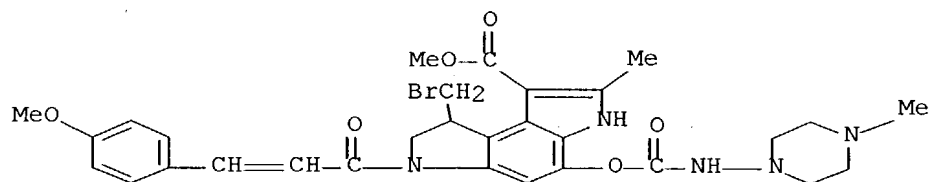
RN 173903-65-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-66-7 CAPLUS

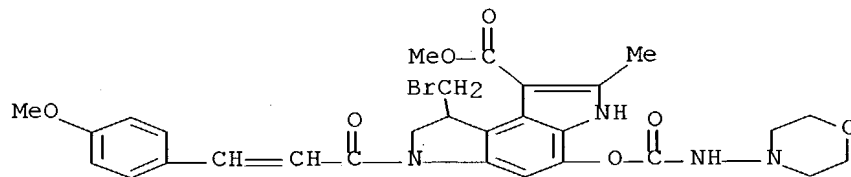
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 173903-67-8 CAPLUS

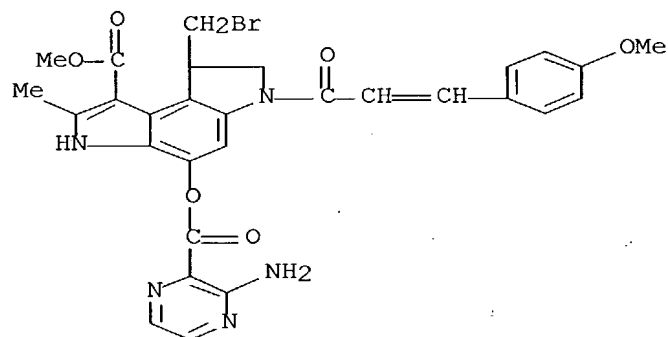
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-morpholinylamino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-68-9 CAPLUS

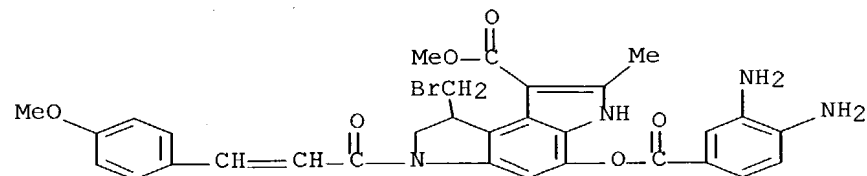
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[3-aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA

INDEX
NAME)



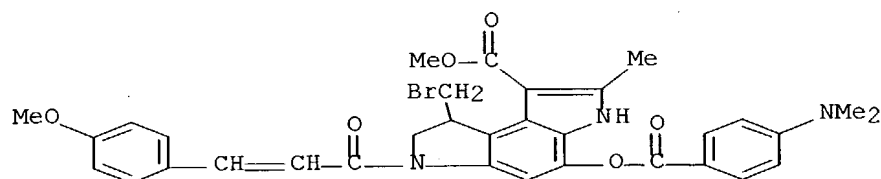
RN 173903-69-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[(3,4-diaminobenzoyl)oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



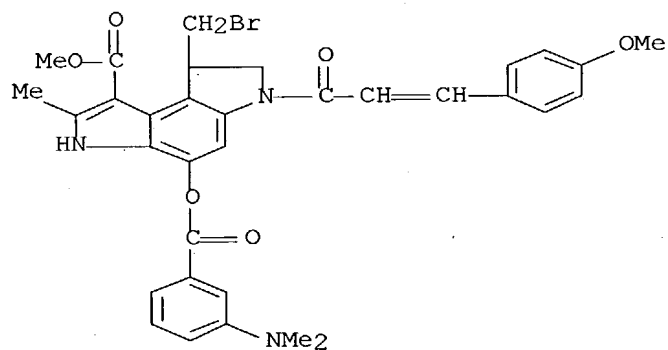
RN 173903-70-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-(dimethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



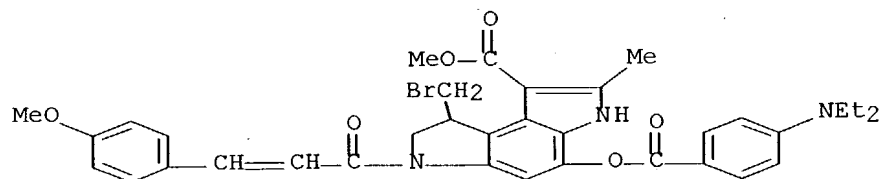
RN 173903-71-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[3-(dimethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



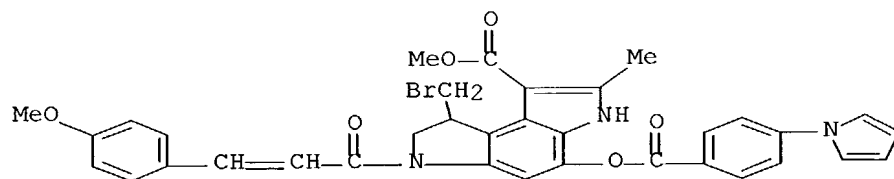
RN 173903-72-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-(diethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



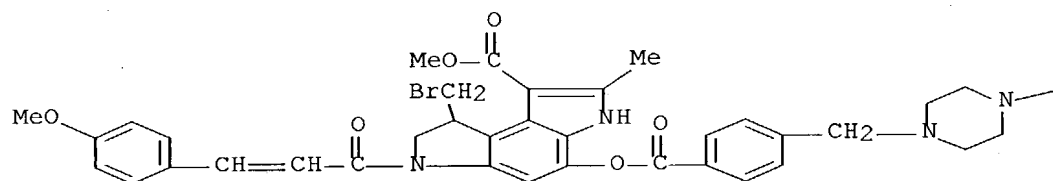
RN 173903-73-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-(1H-pyrrol-1-yl)benzoyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-74-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



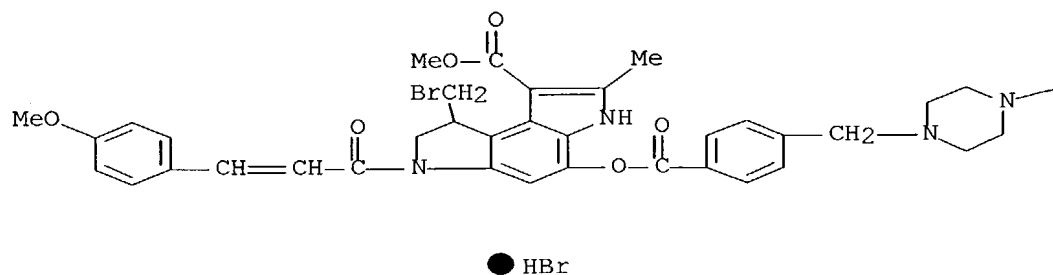
PAGE 1-A

PAGE 1-B

—Me

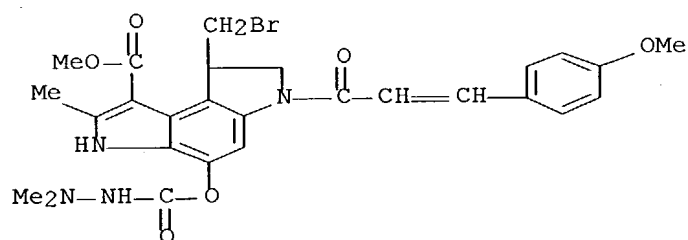
RN 173903-75-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)

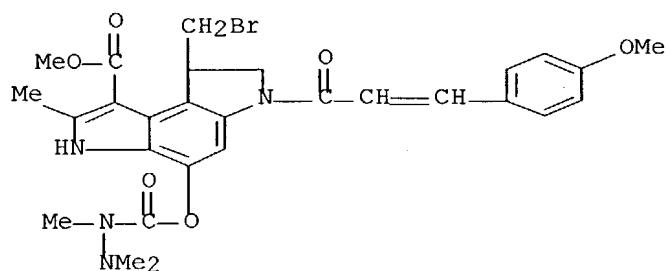


— Me

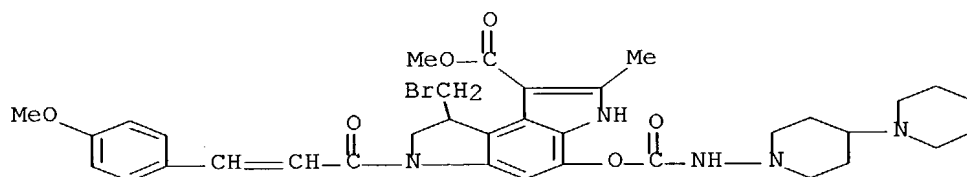
RN 173903-76-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[[2,2-
 dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-
 methoxyphenyl)-
 1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



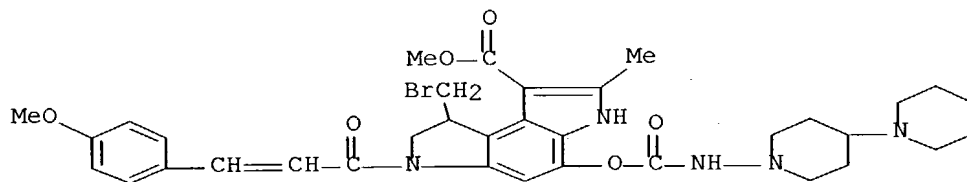
RN 173903-77-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-
 [[[trimethylhydrazino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX
 NAME)



RN 173903-78-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-
 1'-ylamino)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA
 INDEX
 NAME)



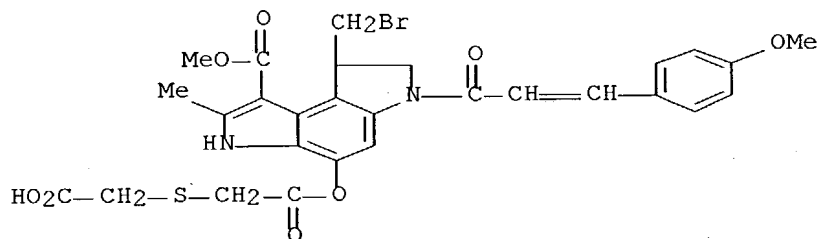
RN 173903-79-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-
 1'-ylamino)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester,
 monohydrobromide
 (9CI) (CA INDEX NAME)



● HBr

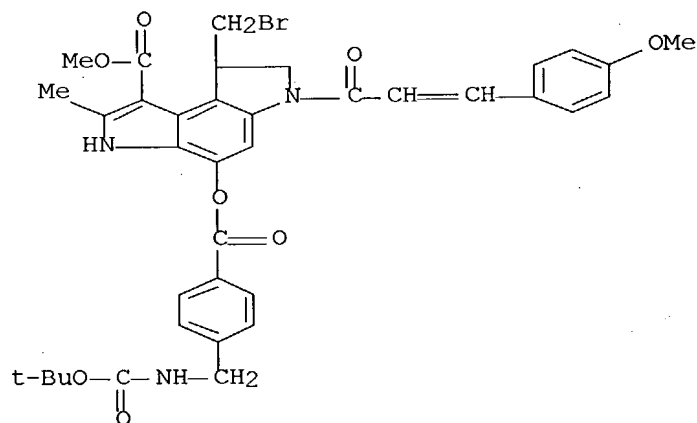
RN 173903-80-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester (9CI) (CA
 INDEX NAME)



RN 173903-81-6 CAPLUS

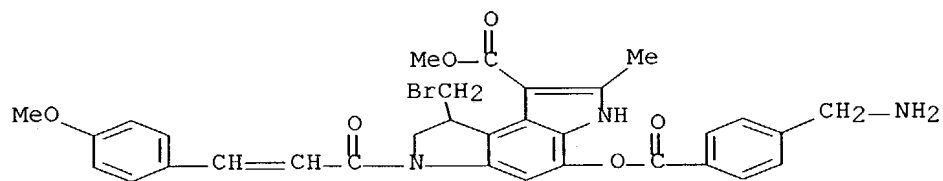
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-
 [[[(1,1-dimethylethoxy)carbonyl]amino]methyl]benzoyl]oxy]-3,6,7,8-
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl
 ester (9CI) (CA INDEX NAME)



RN 173903-82-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-
 (aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA

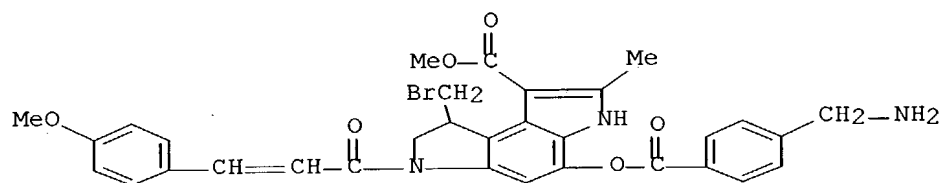
INDEX
 NAME)



RN 173903-83-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrobromide

(9CI) (CA INDEX NAME)

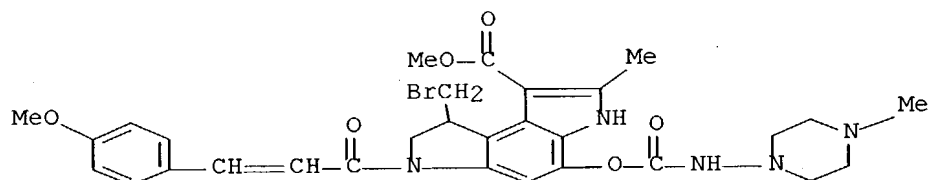


● HBr

RN 173903-84-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrobromide

(9CI) (CA INDEX NAME)

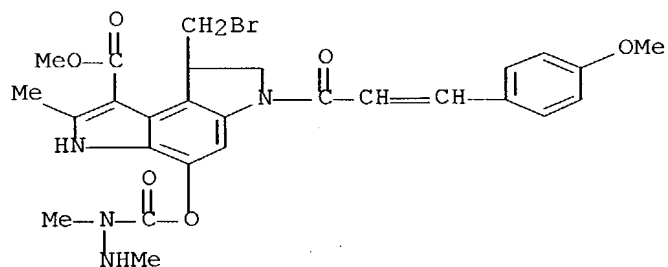


● HBr

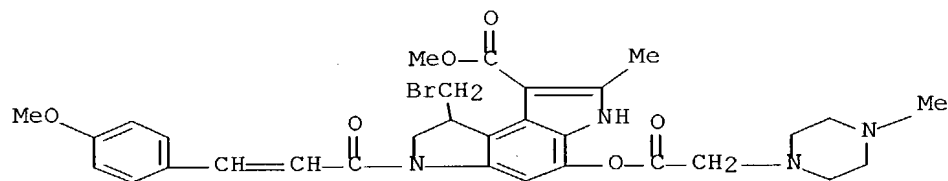
RN 173903-85-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1,2-

dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

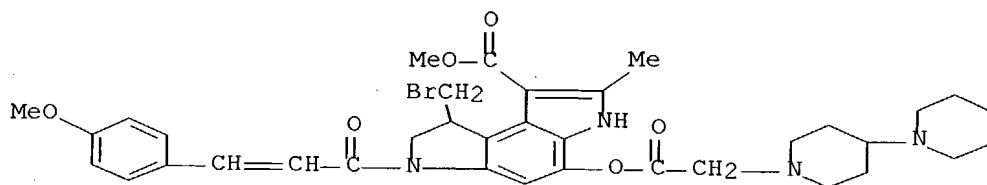


RN 173903-86-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl)acetyl]oxy]-, methyl ester, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

RN 173903-87-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-ylacetyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, dihydrobromide (9CI) (CA INDEX NAME)



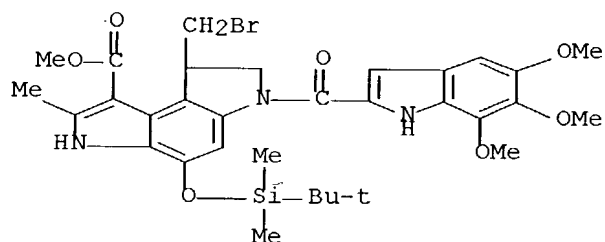
● 2 HBr

IT 134127-18-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of DC-89 (pyrroloindoline) derivs. as antitumor agents)

RN 134127-18-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



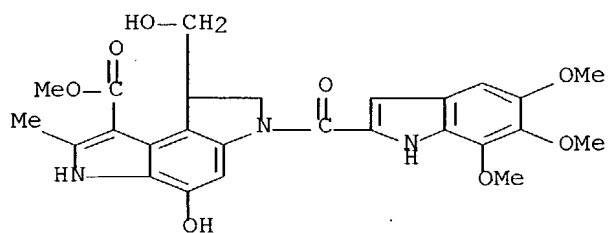
IT 173903-88-3P 173903-89-4P 173903-90-7P
173903-91-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)

(preparation of DC-89 (pyrroloindoline) derivs. as antitumor agents)

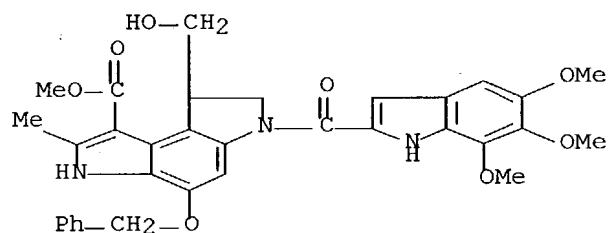
RN 173903-88-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-4-hydroxy-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



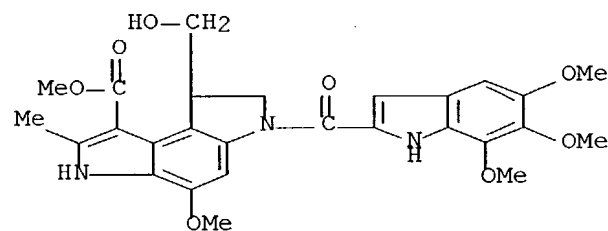
RN 173903-89-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-90-7 CAPLUS

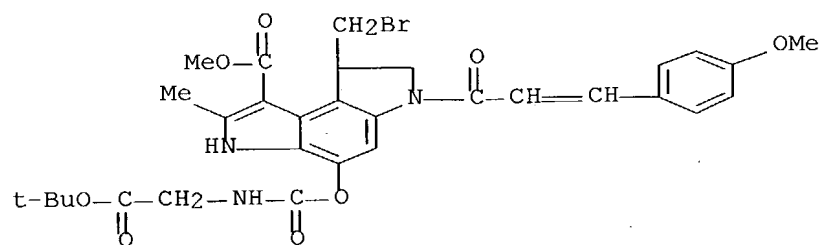
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-91-8 CAPLUS

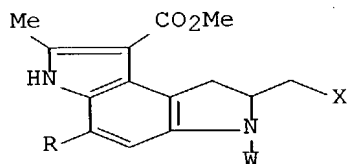
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl]-, methyl ester (9CI)
(CA

INDEX NAME)

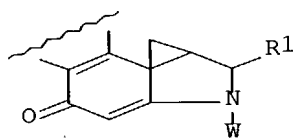


L10 ANSWER 74 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:996496 CAPLUS Full-text
 DN 124:116964
 TI Preparation of DC-89 derivatives as antitumors
 IN Amishiro, Nobuyoshi; Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji;
 Okamoto, Akihiko; Gomi, Katsushige
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO PCT Int. Appl., 93 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9526964	A1	19951012	WO 1995-JP626	19950331
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9520848	A1	19951023	AU 1995-20848	19950331
	AU 689566	B2	19980402		
	EP 702014	A1	19960320	EP 1995-913398	19950331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,				
SE	US 5670492	A	19970923	US 1995-557055	19951128
PRAI	JP 1994-65236		19940401		
	WO 1995-JP626		19950331		
OS	MARPAT 124:116964				
GI					



I



II

AB DC-89 derivs. e.g. I [W = heterocyclalakenoyl, arylalkenoyl, etc.; X = Cl, Br; R = acyloxy, 4-alkylpiperazin-1-ylamino] and II (R1 = H, CH2-X; X and W same as above) and their pharmaceutically acceptable salts, having excellent antitumor activity and useful as antitumor drugs, are prepared Thus, a mixture of II [W = R1 = H] was reacted with p-nitrophenyl (E)-3-(6-methoxy-3-pyridinyl)acrylate in DMF containing NaH at -20° for 2 h to give 78% II [W = (E)-3-(6-methoxy-3-pyridinyl)acryloyl, R1 = H]. This at 1.0 mg/Kg i.v. had an IC50 of 0.42 nM against sarcoma 180 tumors in mice.

IT 173087-75-7P 173087-76-8P 173087-78-0P
 173087-80-4P 173087-82-6P 173087-84-8P
 173087-86-0P 173087-90-6P 173087-93-9P
 173087-95-1P 173087-96-2P 173087-98-4P
 173087-99-5P 173088-00-1P 173088-01-2P
 173088-02-3P 173088-03-4P 173088-04-5P

173088-05-6P 173088-06-7P 173088-07-8P

173088-08-9P 173088-09-0P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

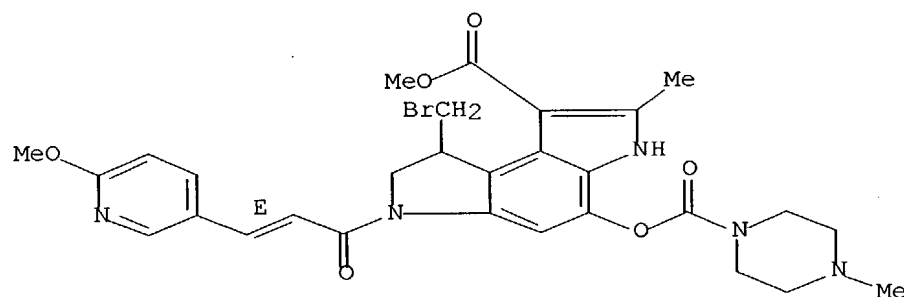
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
(preparation of duocarmycin B1 derivs. as antitumors)

RN 173087-75-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-

[[(4-methyl-1-piperazinyl)carbonyloxy]-, methyl ester, (E)- (9CI) (CA INDEX
NAME)

Double bond geometry as shown.

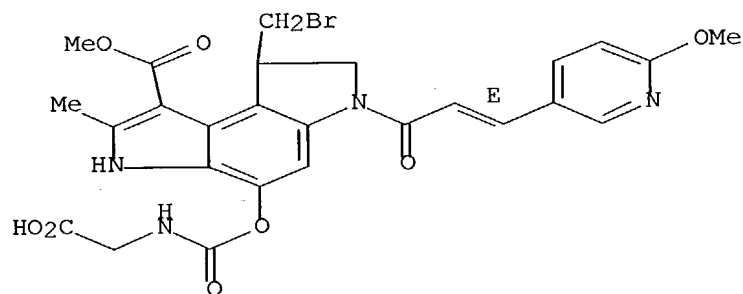


RN 173087-76-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
[[[(carboxymethyl)amino]carbonyloxy]-3,6,7,8-tetrahydro-6-[3-(6-
methoxy-3-

pyridinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI) (CA
INDEX NAME)

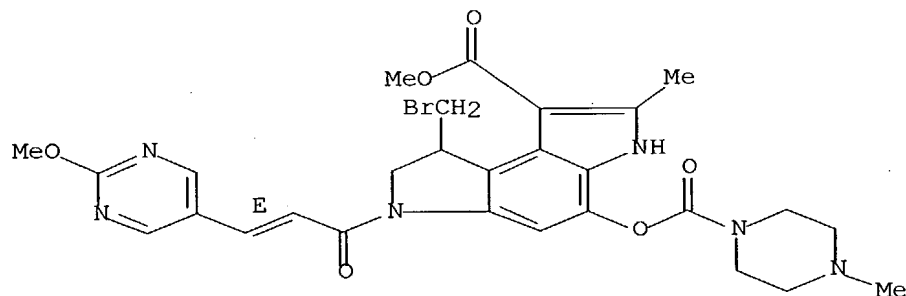
Double bond geometry as shown.



RN 173087-78-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

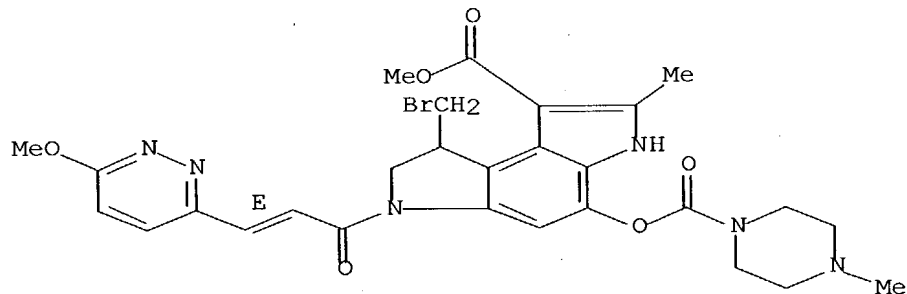
Double bond geometry as shown.



RN 173087-80-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

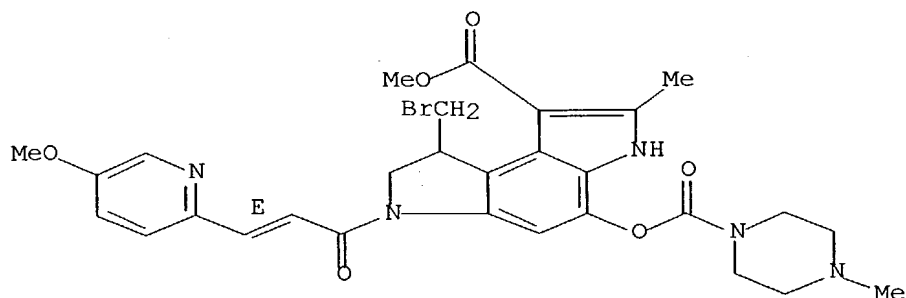
Double bond geometry as shown.



RN 173087-82-6 CAPLUS

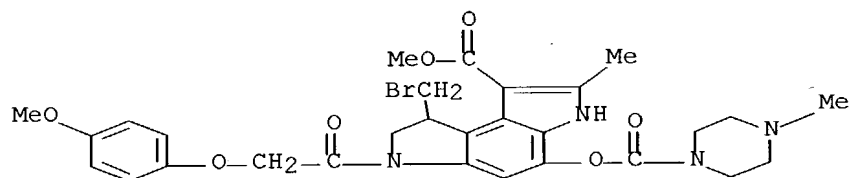
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



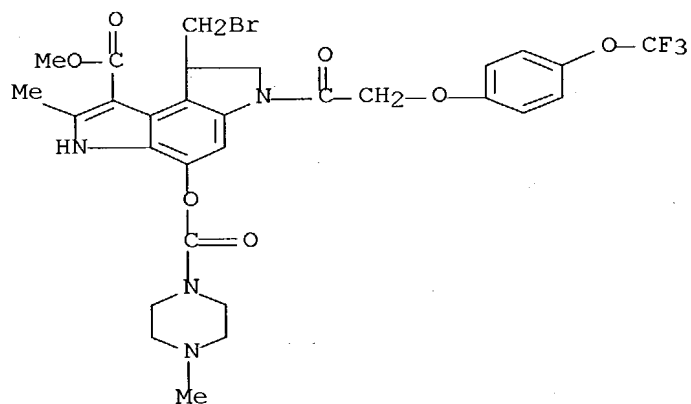
RN 173087-84-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(4-methoxyphenoxy)acetyl]-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 173087-86-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[4-(trifluoromethoxy)phenoxy]acetyl]-, methyl ester (9CI) (CA INDEX NAME)

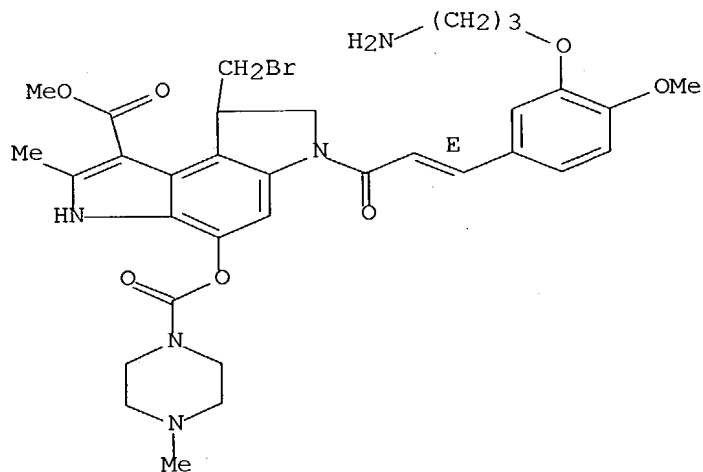


RN 173087-90-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-[3-(3-

aminopropoxy)-4-methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)-(9CI) (CA INDEX NAME)

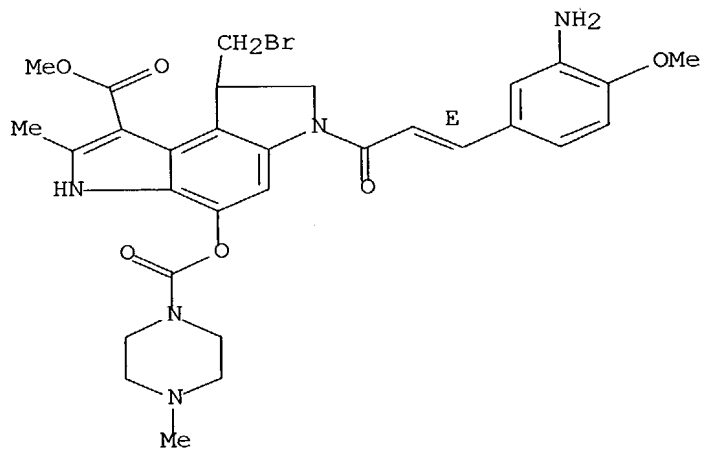
Double bond geometry as shown.



RN 173087-93-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

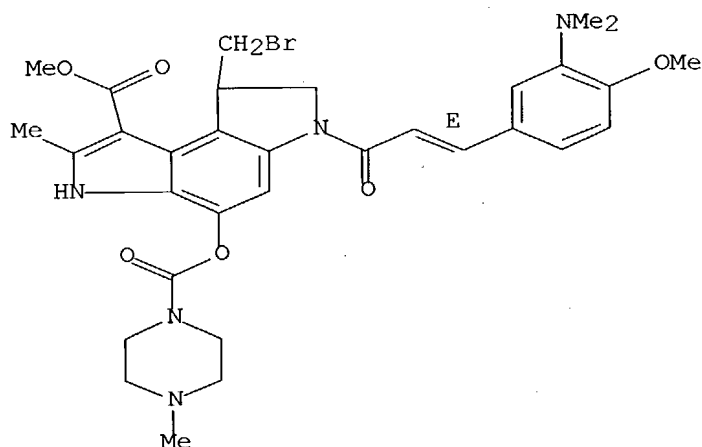


RN 173087-95-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-

methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

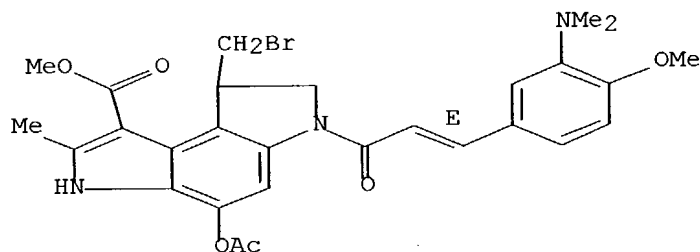


RN 173087-96-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-

3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

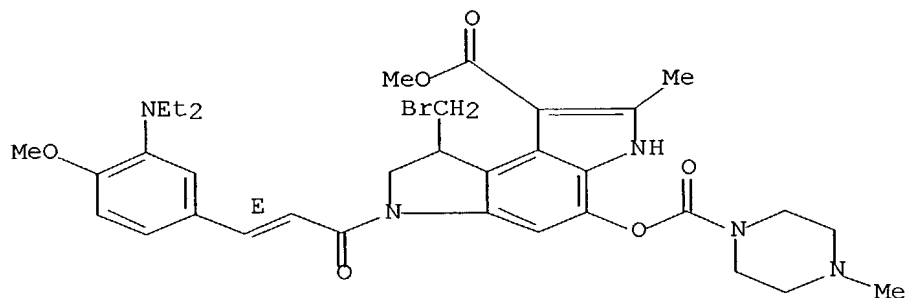
Double bond geometry as shown.



RN 173087-98-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

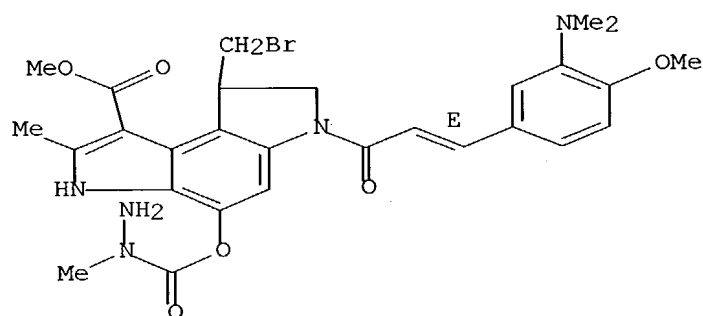
Double bond geometry as shown.



RN 173087-99-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, (E)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

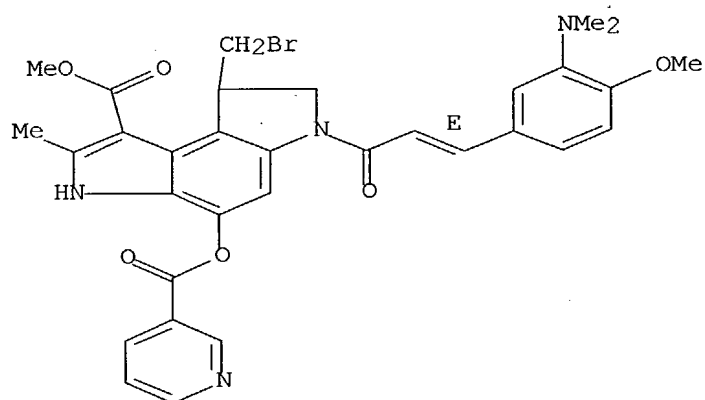


RN 173088-00-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (E)- (9CI) (CA

INDEX
NAME)

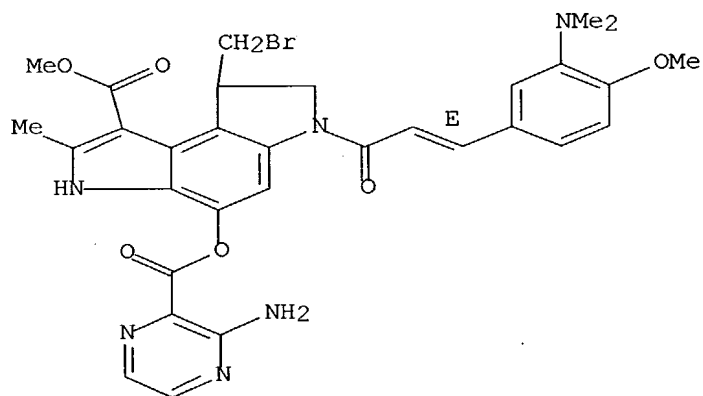
Double bond geometry as shown.



RN 173088-01-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[3-aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

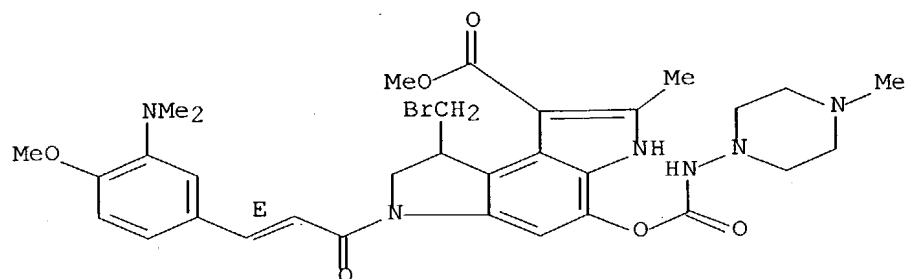
Double bond geometry as shown.



RN 173088-02-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

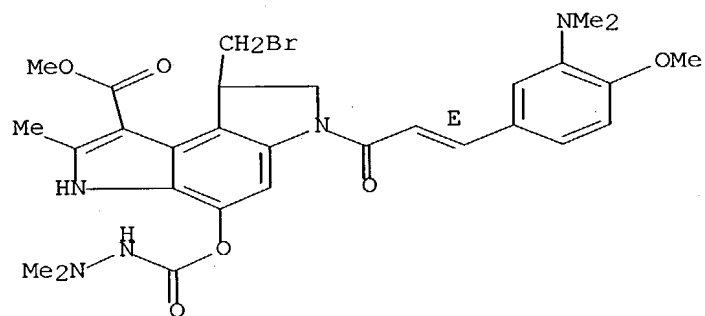
Double bond geometry as shown.



RN 173088-03-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[2,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

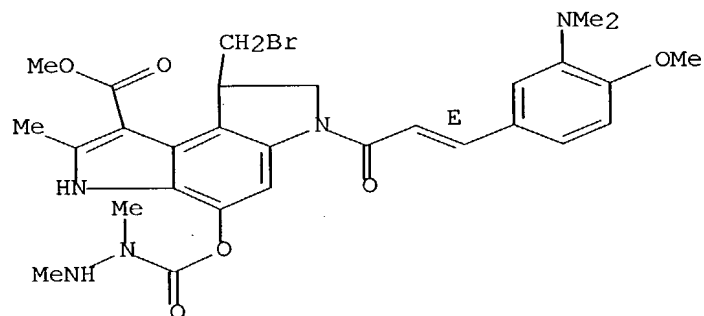
Double bond geometry as shown.



RN 173088-04-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[2,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

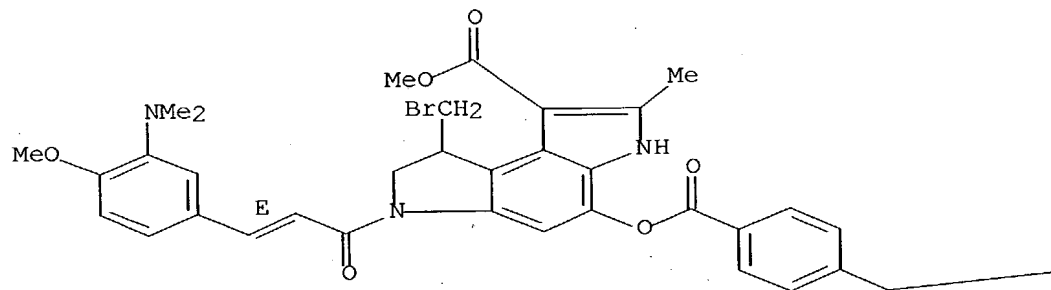


RN 173088-05-6 CAPLUS

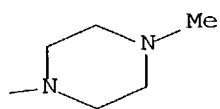
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



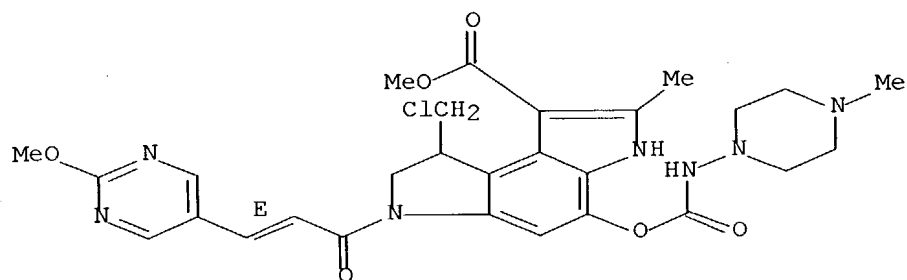
PAGE 1-B



RN 173088-06-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (E)-
(9CI)
(CA INDEX NAME)

Double bond geometry as shown.

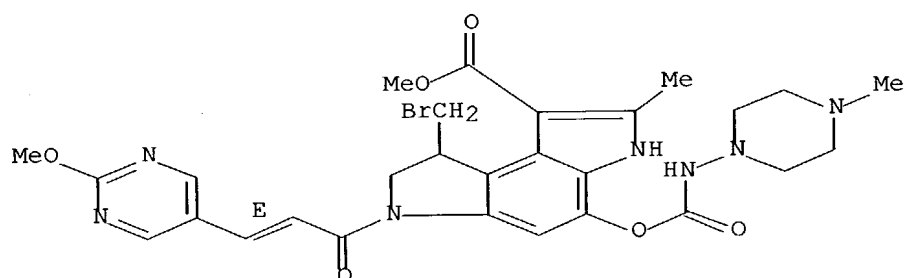


RN 173088-07-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (E)- (9CI)

(CA INDEX NAME)

Double bond geometry as shown.



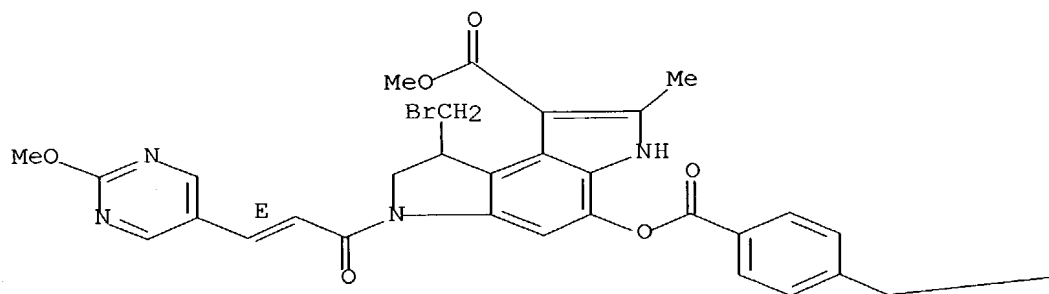
RN 173088-08-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-

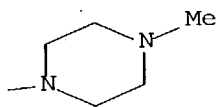
[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (E)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

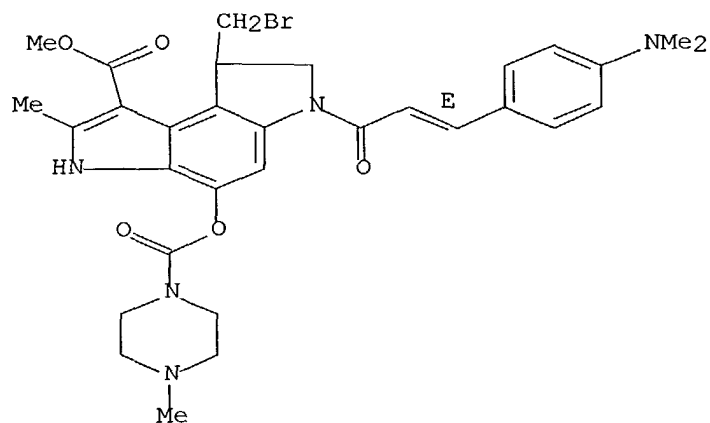


PAGE 1-B



RN 173088-09-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 173088-10-3P 173088-11-4P 173088-12-5P
 173088-13-6P 173088-14-7P 173088-15-8P
 173088-16-9P 173088-17-0P 173088-18-1P
 173088-21-6P 173088-24-9P 173088-27-2P
 173088-28-3P 173088-29-4P 173088-30-7P
 173088-31-8P 173088-32-9P 173088-33-0P
 173088-34-1P 173088-35-2P 173088-36-3P
 173088-37-4P 173088-38-5P 173088-39-6P
 173088-40-9P 173088-41-0P 173088-42-1P
 173088-43-2P 173088-44-3P 173088-45-4P
 173088-46-5P 173088-47-6P 173088-48-7P
 173088-49-8P 173088-50-1P 173088-51-2P
 173088-52-3P 173088-53-4P 173088-54-5P
 173088-55-6P 173088-56-7P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of duocarmycin B1 derivs. as antitumors)

RN 173088-10-3 CAPLUS

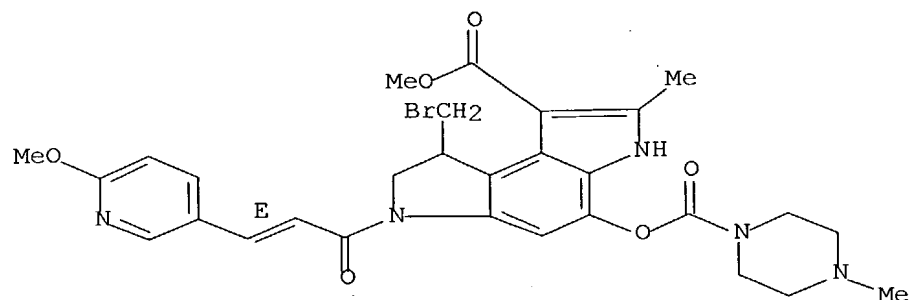
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-

[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride,

(E)-

(9CI) (CA INDEX NAME)

Double bond geometry as shown.



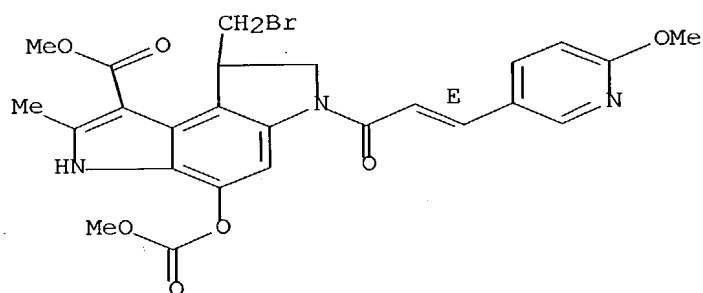
● HCl

RN 173088-11-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-

2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

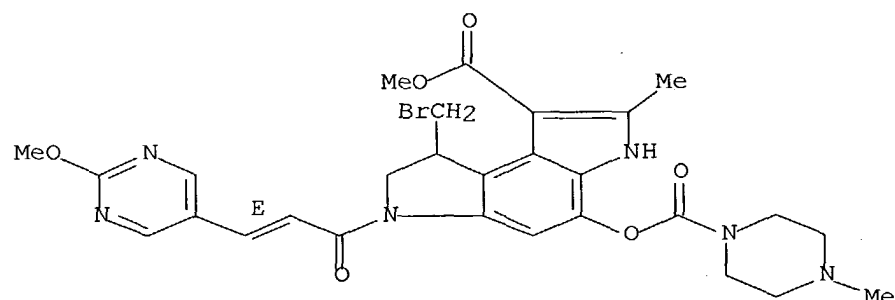


RN 173088-12-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,

monohydrochloride,
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



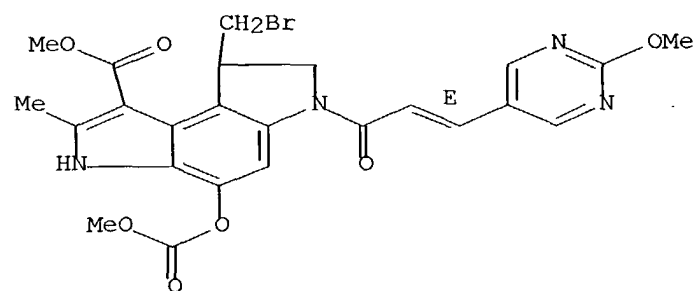
● HCl

RN 173088-13-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-

propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



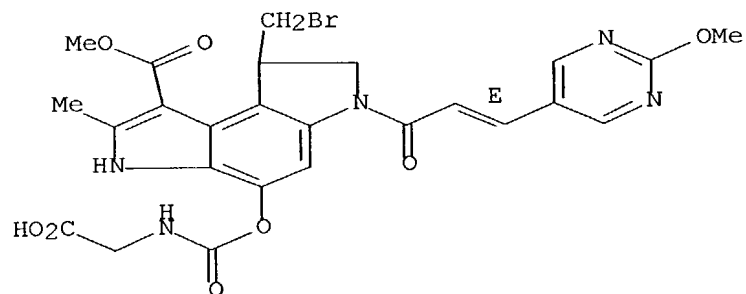
RN 173088-14-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-

pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI)

(CA INDEX NAME)

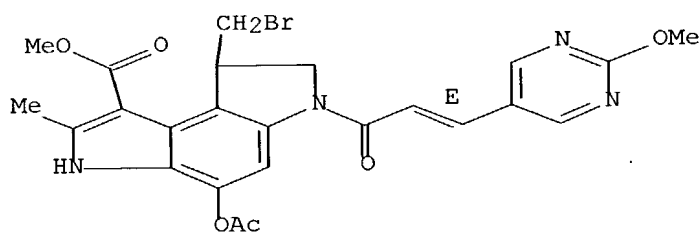
Double bond geometry as shown.



RN 173088-15-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

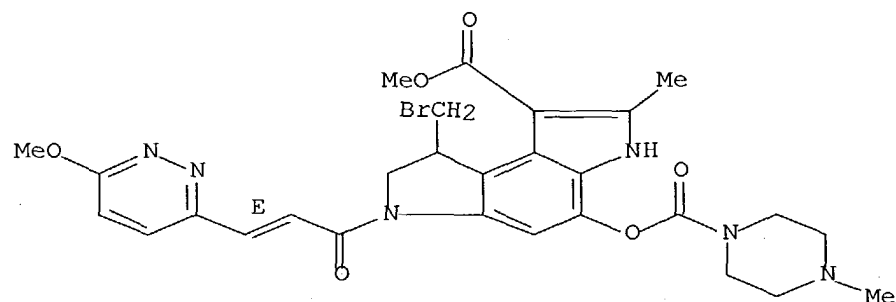
Double bond geometry as shown.



RN 173088-16-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

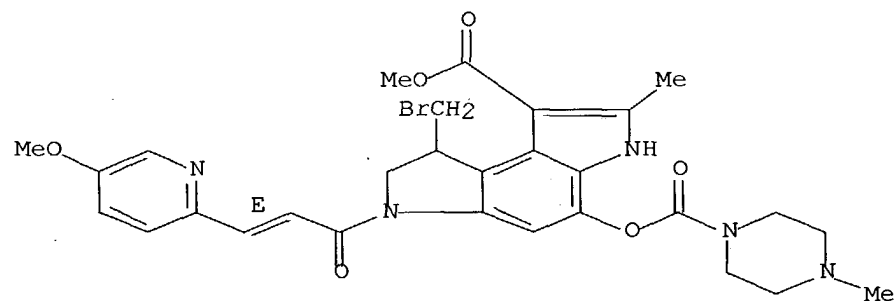


● HCl

RN 173088-17-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

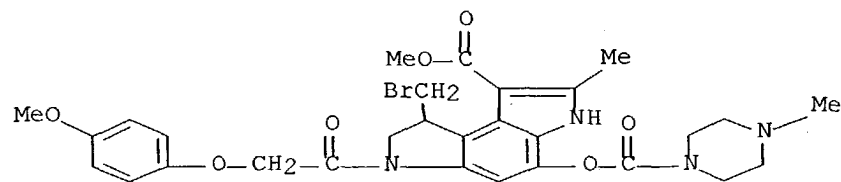
Double bond geometry as shown.



● HCl

RN 173088-18-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(4-methoxyphenoxy)acetyl]-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



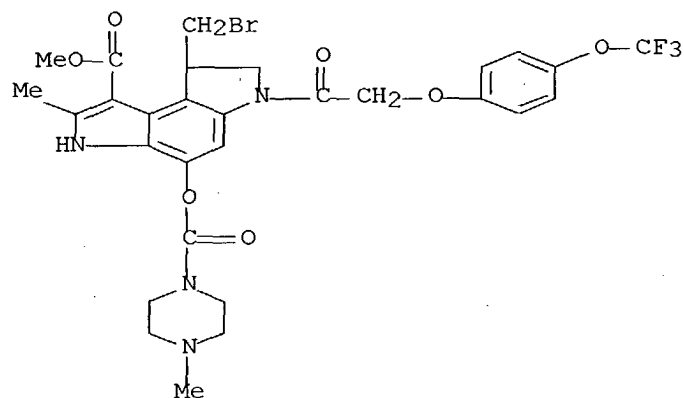
● HCl

RN 173088-21-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[4-(trifluoromethoxy)phenoxy]acetyl]-, methyl ester, monohydrochloride

(9CI)

(CA INDEX NAME)

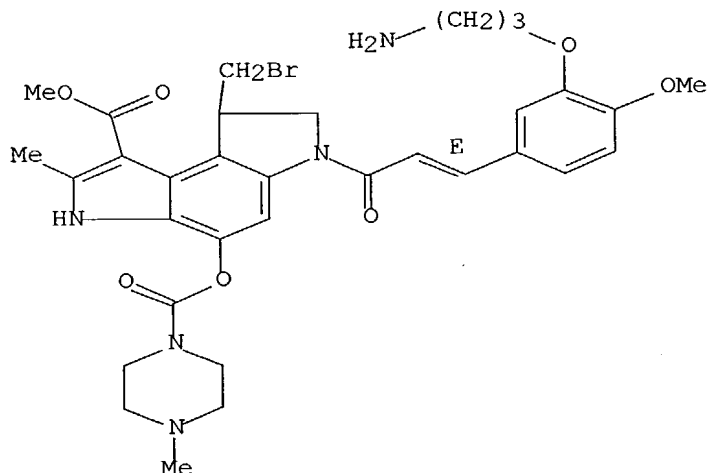


● HCl

RN 173088-24-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-[3-(3-aminopropoxy)-4-methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

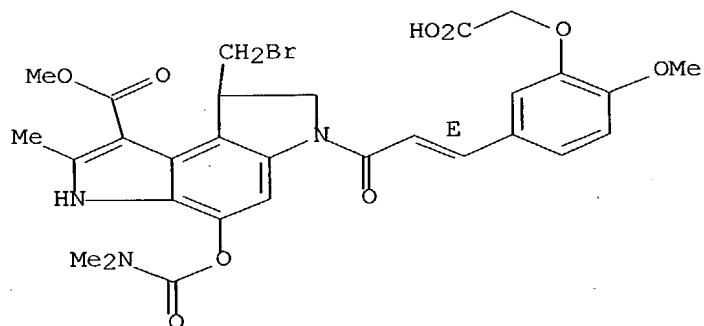
Double bond geometry as shown.



●2 HCl

RN 173088-27-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(carboxymethyl)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (E)- (9CI) (CA INDEX NAME)

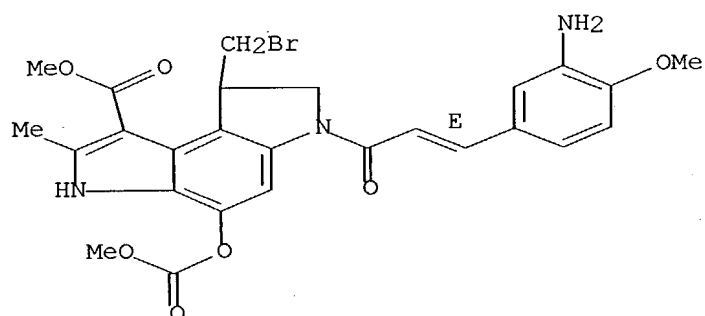
Double bond geometry as shown.



RN 173088-28-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-

[(methoxycarbonyl)oxy]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

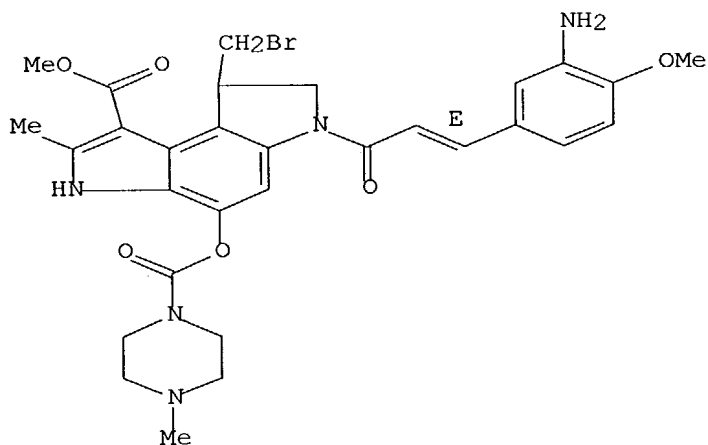


RN 173088-29-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



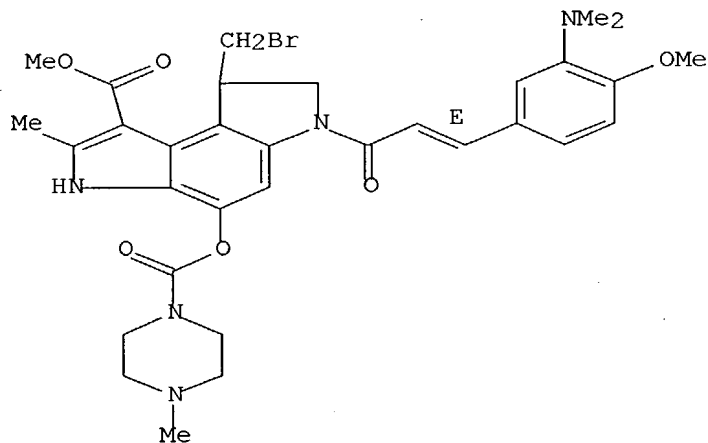
PAGE 2-A

RN 173088-30-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



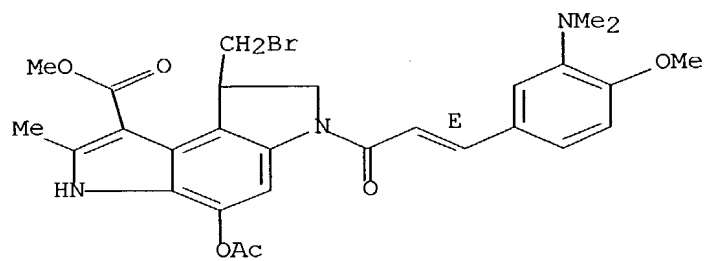
PAGE 2-A

● 2 HCl

RN 173088-31-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

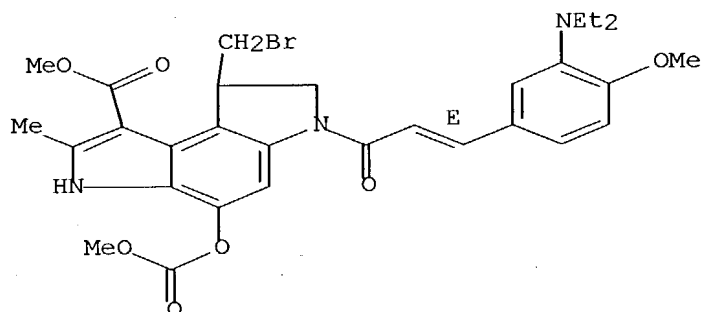


● HCl

RN 173088-32-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

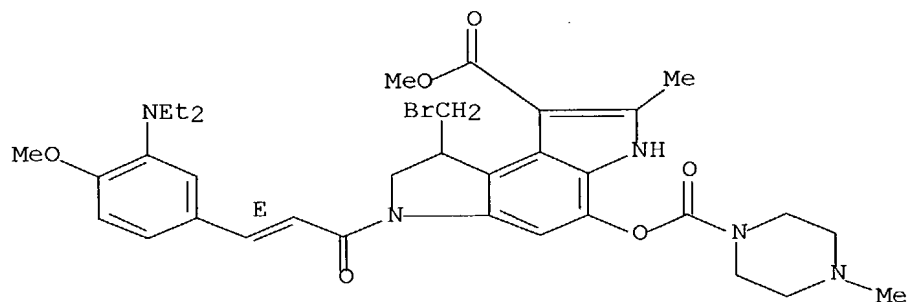
Double bond geometry as shown.



RN 173088-33-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

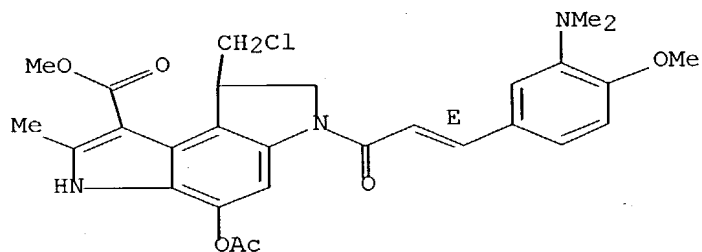
Double bond geometry as shown.



● 2 HCl

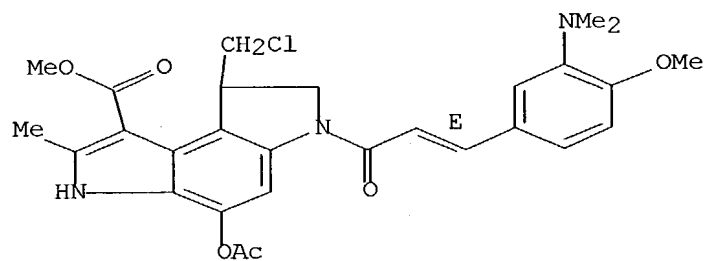
RN 173088-34-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-
 3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 173088-35-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-
 3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrochloride, (E)- (9CI)
 (CA INDEX NAME)

Double bond geometry as shown.

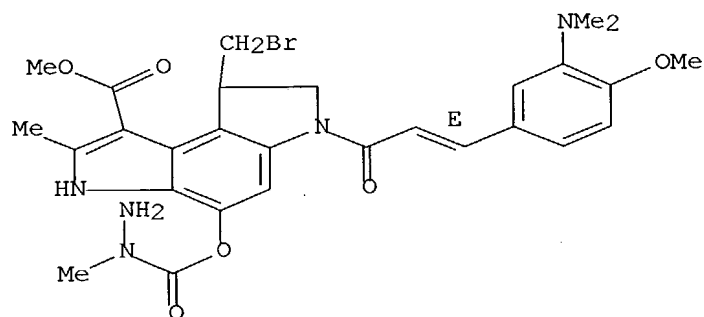


● HCl

RN 173088-36-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[1-(1-methylhydrazino)carbonyl]oxy]-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

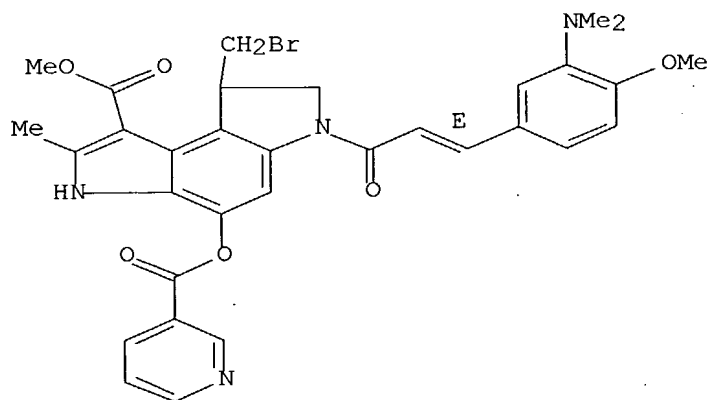


● HBr

RN 173088-37-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

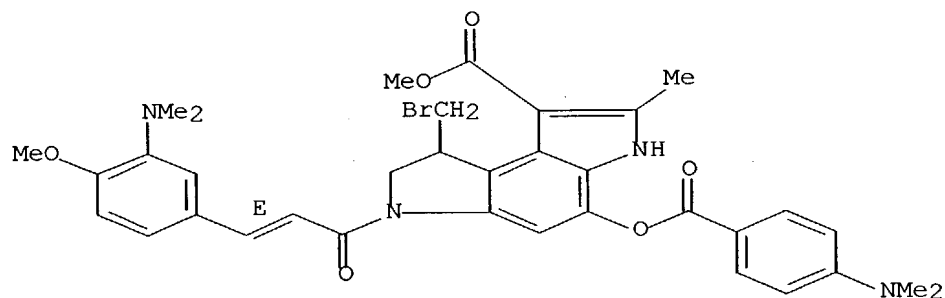
Double bond geometry as shown.



● 2 HBr

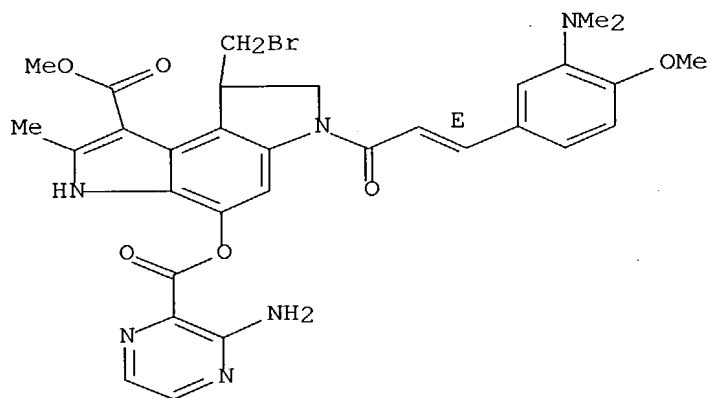
RN 173088-38-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-(dimethylamino)benzoyl]oxy]-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 173088-39-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[3-aminopyrazinyl]carbonyl]oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

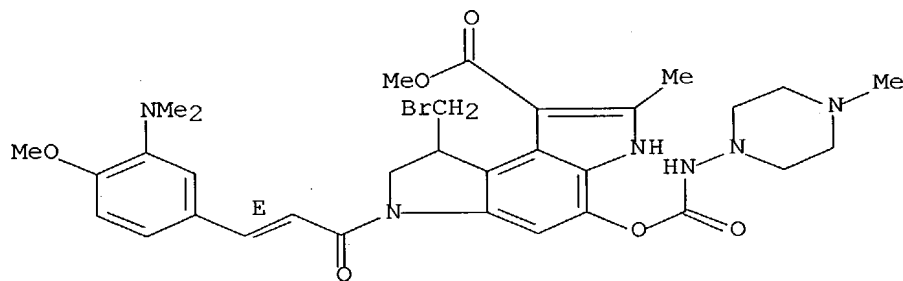


●2 HBr

RN 173088-40-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

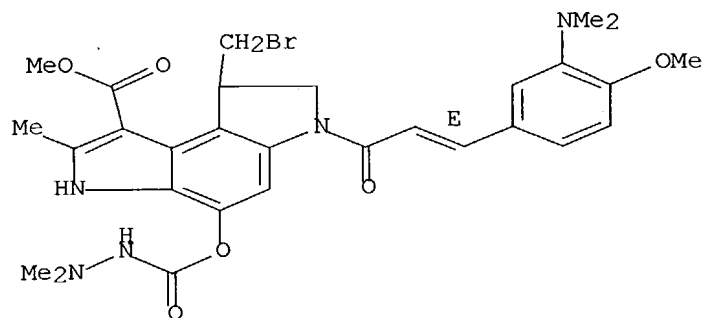


●2 HBr

RN 173088-41-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[[(2,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

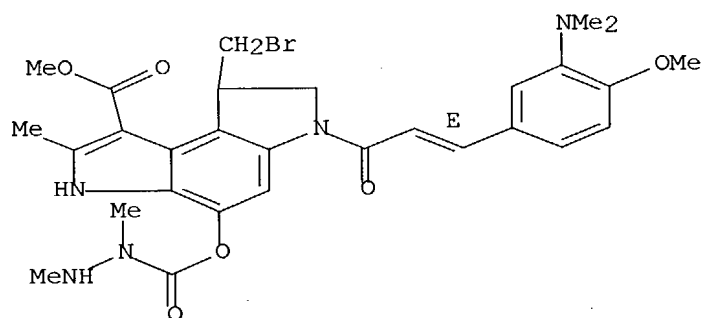


● HBr

RN 173088-42-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[1,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



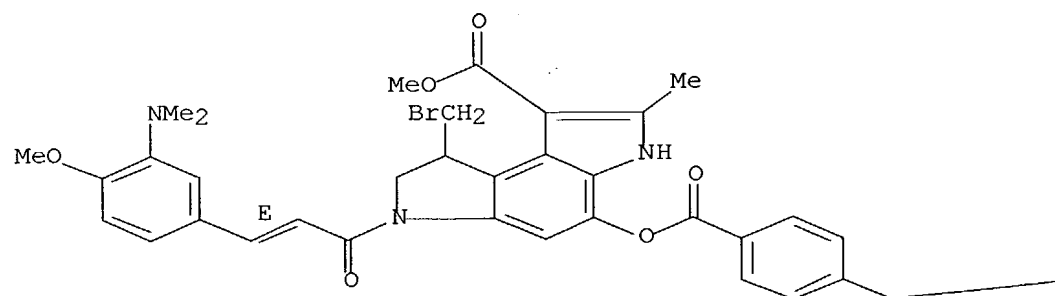
● HBr

RN 173088-43-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

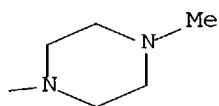
Double bond geometry as shown.

PAGE 1-A



●2 HBr

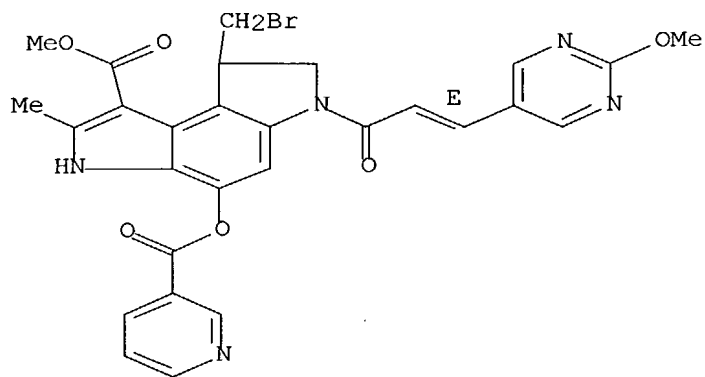
PAGE 1-B



RN 173088-44-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

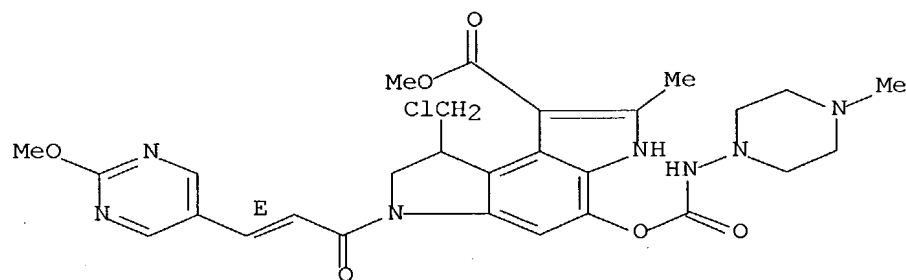


RN 173088-45-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

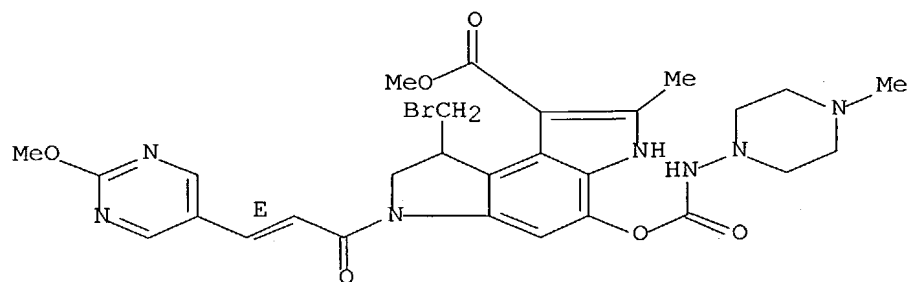


● HCl

RN 173088-46-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

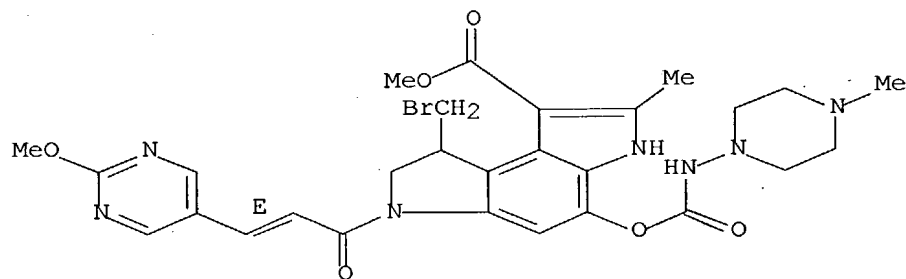


● HCl

RN 173088-47-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



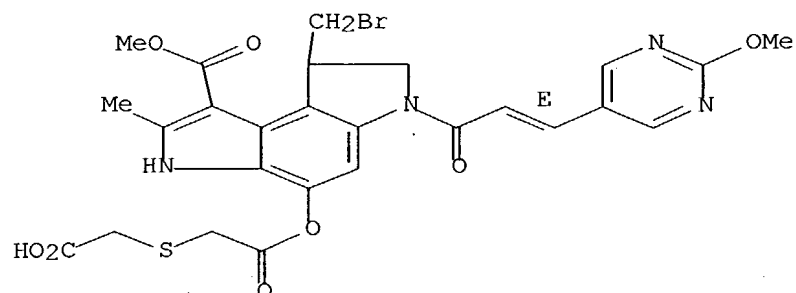
● HBr

RN 173088-48-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI)

(CA INDEX NAME)

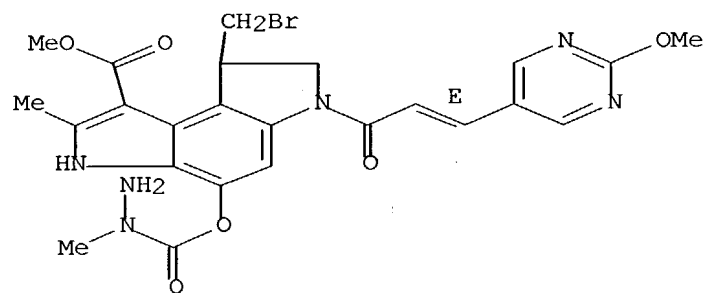
Double bond geometry as shown.



RN 173088-49-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1-methylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

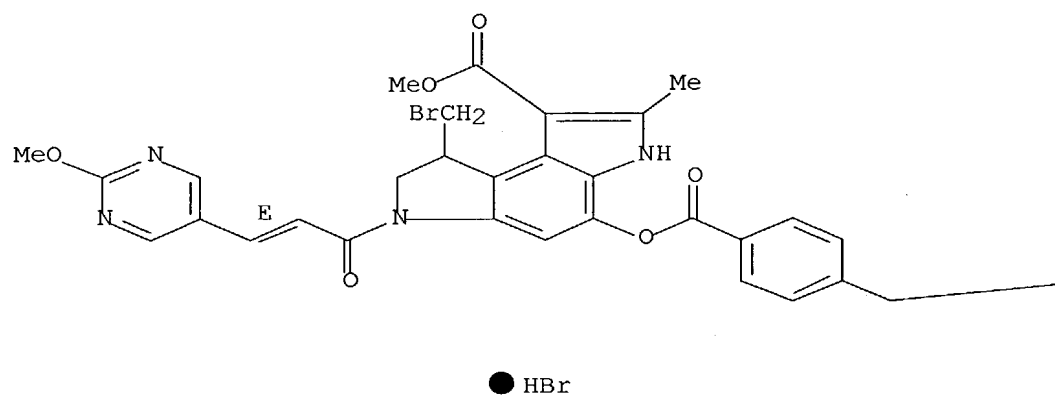


RN 173088-50-1 CAPLUS

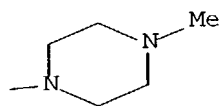
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-(4-methyl-1-piperazinyl)methyl]benzoyl]oxy-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



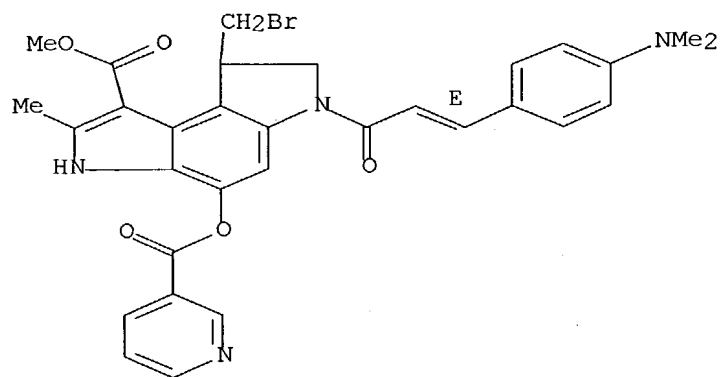
PAGE 1-B



RN 173088-51-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

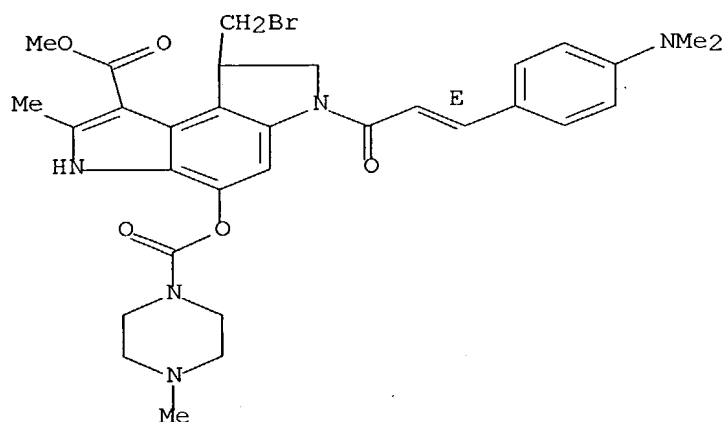


RN 173088-52-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrobromide,
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

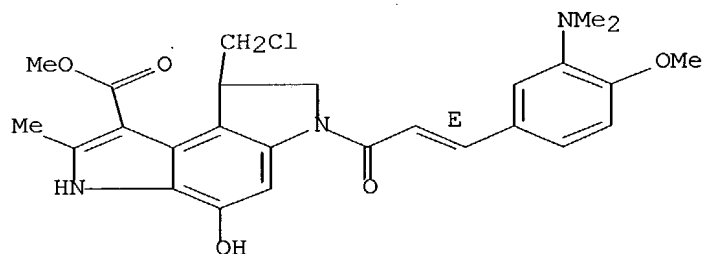
● HBr

RN 173088-53-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-

hydroxy-2-methyl-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

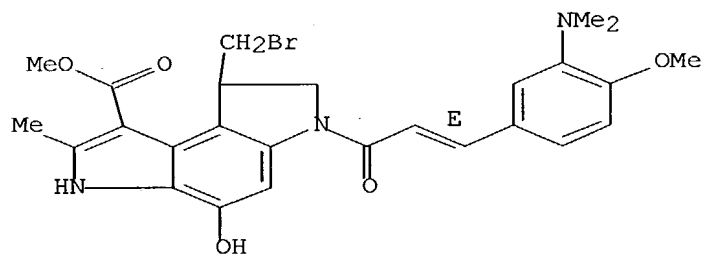
Double bond geometry as shown.



● HCl

RN 173088-54-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

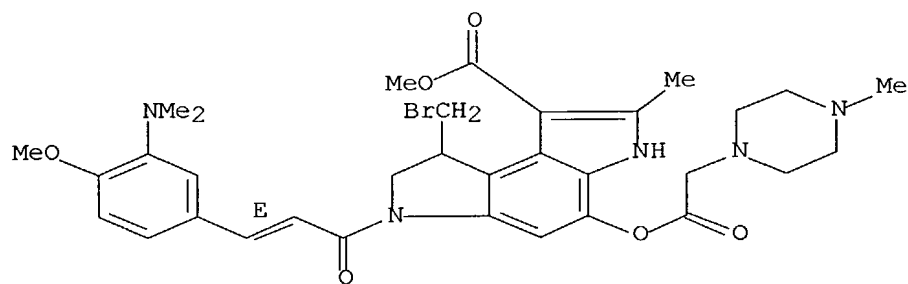
Double bond geometry as shown.



● HBr

RN 173088-55-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]acetyl]oxy-, methyl ester, trihydrobromide, (E)- (9CI) (CA INDEX NAME)

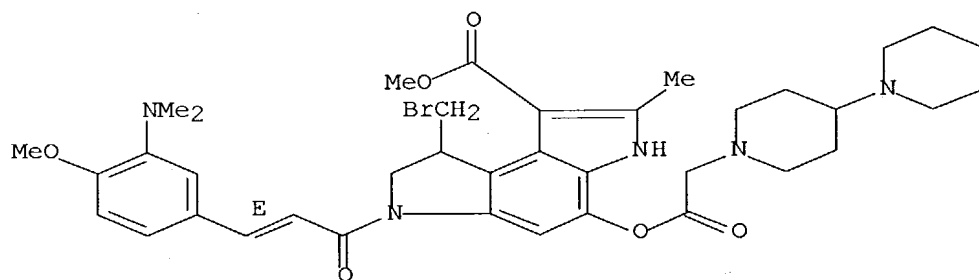
Double bond geometry as shown.



●3 HBr

RN 173088-56-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-
 1'-ylacetyl)oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-
 1-oxo-2-propenyl]-2-methyl-, methyl ester, trihydrobromide, (E)- (9CI)
 (CA INDEX NAME)

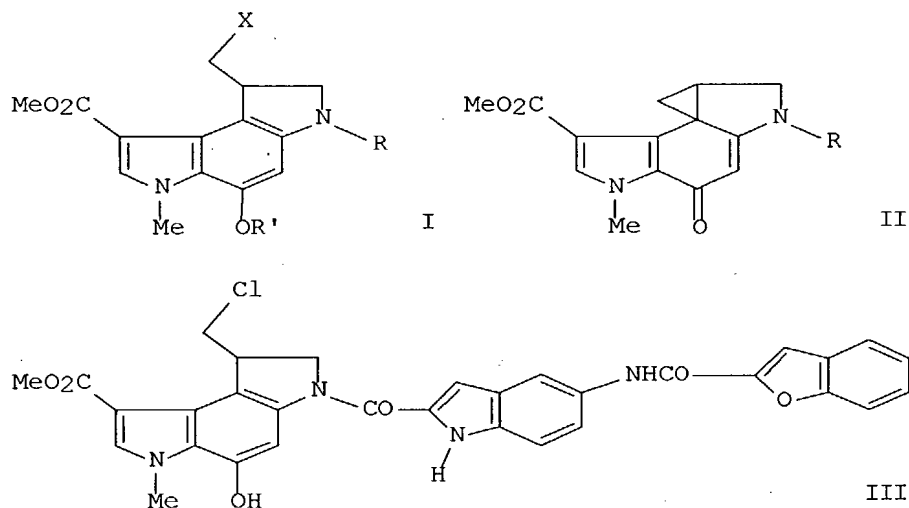
Double bond geometry as shown.



●3 HBr

L10 ANSWER 75 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:926111 CAPLUS Full-text
 DN 123:340084
 TI Pyrrolo[3,2-e]indole derivatives, process for their preparation, and applications as antitumor agents
 IN Delamano Garcia, Jose; Tojo Suarez, Gabriel; Lopez Goti, Carmen; Fernandez Almeida, Jesus; Garcia Gravalos, Dolores; Faircloth, Glynn Thomas
 PA Universidad de Santiago de Compostela, Spain
 SO PCT Int. Appl., 45 pp.
 CODEN: PIXXD2
 DT Patent
 LA Spanish
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9514022	A1	19950526	WO 1994-ES122	19941118
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ES 2074957	A1	19950916	ES 1993-2430	19931119
	ES 2074957	B1	19960616		
	EP 680964	A1	19951108	EP 1995-900773	19941118
	EP 680964	B1	20020116		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
SE	JP 08509990	T2	19961022	JP 1994-514236	19941118
	AT 212023	E	20020215	AT 1995-900773	19941118
	PT 680964	T	20020628	PT 1995-95900773	19941118
	ES 2171521	T3	20020916	ES 1995-900773	19941118
	US 5786377	A	19980728	US 1997-790904	19970129
PRAI	ES 1993-2430	A	19931119		
	ES 1993-243	A	19930209		
	WO 1994-ES122	W	19941118		
	US 1996-491870	A1	19960515		
OS	CASREACT 123:340084; MARPAT 123:340084				
GI					



AB New pyrrolo[3,2-e]indole derivs. of formulas I and II are claimed [wherein R = COR''; R'' = (un)substituted aryl or heteroaryl; R' = H, (un)substituted alkanoyl, alkenoyl, alkynoyl, (hetero)arenocarbonyl; X = Cl, bromo, iodo, alkyl- or arylsulfonyl]. The compds. are prepared by: (a) deacetylating II (R = Ac) to give II (R = H); (b) subjecting the latter to a cyclopropyl ring-opening reaction to give I.HX (R = R' = H); (c) reacting this with an acid R''CO₂H to yield I (R = COR'', R' = H); (d) optionally reacting I with a base in the presence of a condensing agent to obtain II; (e) optionally reacting I with a carboxylic acid in the presence of a condensing agent or with an acid chloride in the presence of a base to give I (R' = acyl). I and II are useful as antitumor agents. For example, deacylation of II (R = Ac) with NaOMe in MeOH gave 99% II (R = H), which was cleaved by anhydrous HCl in EtOAc to give 93% I.HCl (R = R' = H, X = Cl). Coupling of this with 5-[(benzofuran-2-ylcarbonyl)amino]-1H-indole-2-carboxylic acid in DMF in the presence of EtN:C:N(CH₂)₃NMe₂.HCl gave 69% title compound III. In the P388 tumor model in mice, III at 0.5 mg/kg/day i.p. for 9 days gave at treated/control survival ratio of > 391%.

IT **170431-06-8P**

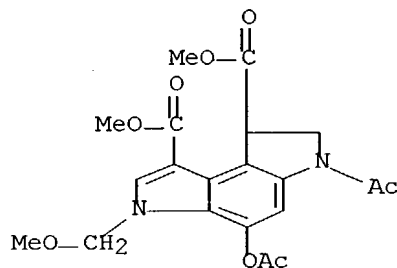
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(byproduct; preparation of pyrroloindole derivs. as antitumor agents)

RN 170431-06-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-

1,2,3,6-tetrahydro-6-(methoxymethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



IT **170430-99-6P 170431-00-2P 170431-01-3P
170431-02-4P 170431-05-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

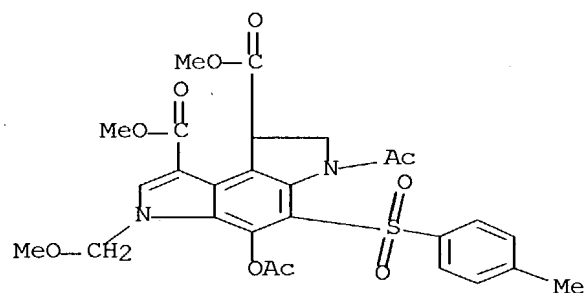
(Reactant or reagent)

(intermediate; preparation of pyrroloindole derivs. as antitumor agents)

RN 170430-99-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-

1,2,3,6-tetrahydro-6-(methoxymethyl)-4-[(4-methylphenyl)sulfonyl]-,
dimethyl ester (9CI) (CA INDEX NAME)

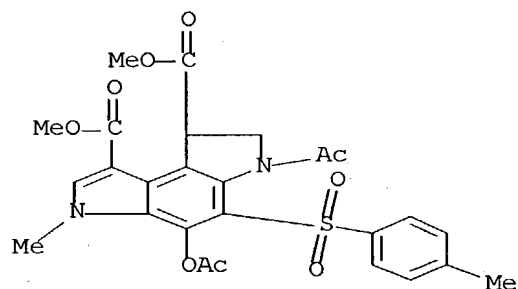


RN 170431-00-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-

1,2,3,6-tetrahydro-6-methyl-4-[(4-methylphenyl)sulfonyl]-, dimethyl ester

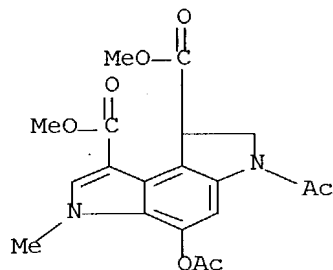
(9CI) (CA INDEX NAME)



RN 170431-01-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-

1,2,3,6-tetrahydro-6-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

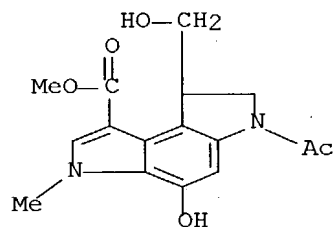


RN 170431-02-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-acetyl-3,6,7,8-tetrahydro-4-hydroxy-8-(hydroxymethyl)-3-methyl-, methyl ester (9CI)

(CA

INDEX NAME)

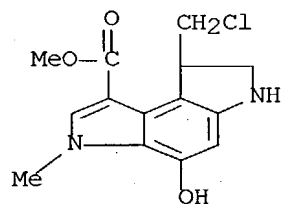


RN 170431-05-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-3-methyl-, methyl ester, monohydrochloride (9CI)

(CA

INDEX NAME)



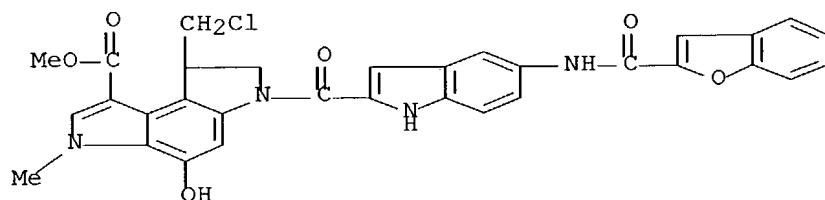
● HCl

IT 170430-92-9P 170430-94-1P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
(preparation of pyrroloindole derivs. as antitumor agents)

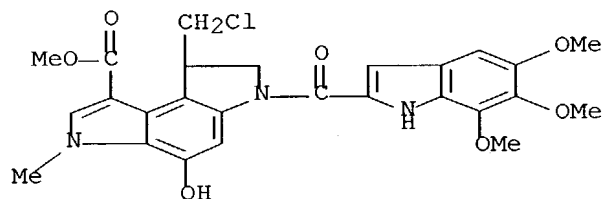
RN 170430-92-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-3-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 170430-94-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-3-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

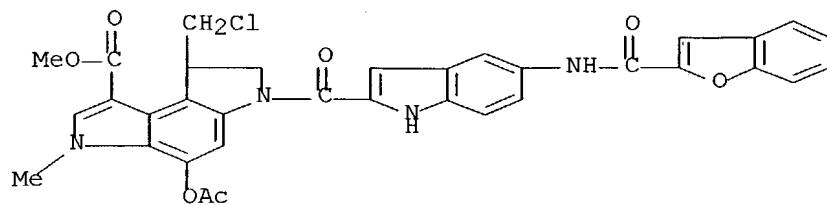


IT 170430-96-3P 170430-97-4P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrroloindole derivs. as antitumor agents)

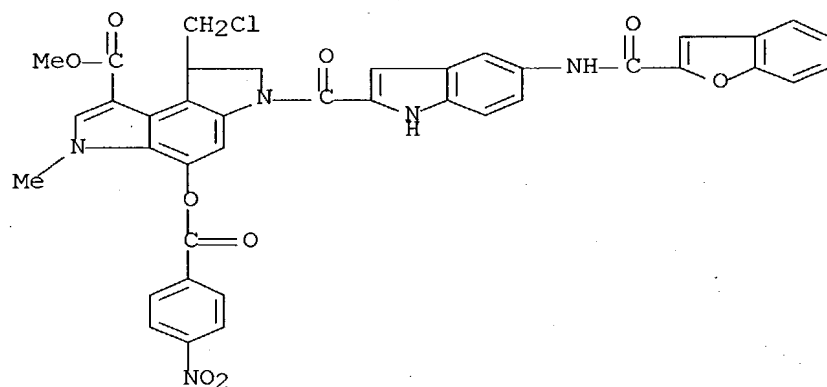
RN 170430-96-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-3-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 170430-97-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-3-methyl-4-[(4-nitrobenzoyl)oxy]-, methyl ester (9CI)
(CA INDEX NAME)



L10 ANSWER 76 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:902197 CAPLUS Full-text

DN 124:29479

TI Synthesis and antitumor activity of duocarmycin derivatives

AU Nagamura, Satoru; Kanda, Yutaka; Kobayashi, Eiji; Gomi, Katsushige; Saito,

Hiromitsu

CS Kyowa Hakko Kogyo Co., Ltd., Tokyo Res. Lab., Tokyo, 194, Japan

SO Chemical & Pharmaceutical Bulletin (1995), 43(9), 1530-5

CODEN: CPBTAL; ISSN: 0009-2363

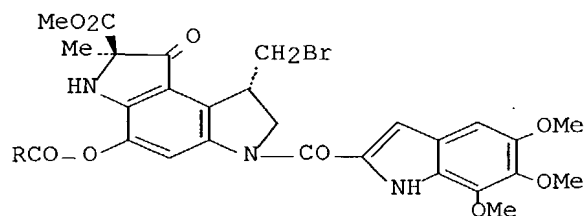
PB Pharmaceutical Society of Japan

DT Journal

LA English

OS CASREACT 124:29479

GI



I

AB A series of duocarmycin B2 derivs. I [R = morpholino-, 4-Mepiperazinyl-CO(CH₂)_n, morpholinyl(CH₂)_n, PhCH₂OCONH(CH₂)_n, Me₂N, 4-Mepiperazinyl, morpholino, piperazinyl, pyrrolidinyl, MeNH, PhNH; n = 1-4], modified at the phenolic hydroxyl group to ester, carbonate and carbamate, was synthesized. Antitumor activity of these analogs was preliminarily evaluated by assays of growth inhibition of HeLa S3 cells (in vitro) and antitumor activity against murine sarcoma 180 (in vivo). The stability of the compds. under aqueous conditions was examined, and we found a correlation between antitumor activity in vivo and stability in aqueous solution, i.e., the more stable derivs. exhibited higher antitumor activity. Among these derivs., the N,N-dialkylcarbamoyle analogs exhibited both improved antitumor activity and higher stability compared with duocarmycin B2. These analogs were subjected to further biol. evaluation and they expressed broad-spectrum activity toward murine solid tumors M5076, Colon 26 and Colon 38, and human xenografted carcinoma MX-1.

IT 154901-65-2P 171524-41-7P 171524-44-0P
171599-18-1P 171599-19-2P 171599-20-5P
171599-21-6P 171599-22-7P 171599-23-8P
171599-25-0P 171599-26-1P 171599-27-2P
171599-29-4P 171599-30-7P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); PRP (Properties); SPN (Synthetic preparation);

BIOL

(Biological study); PREP (Preparation)

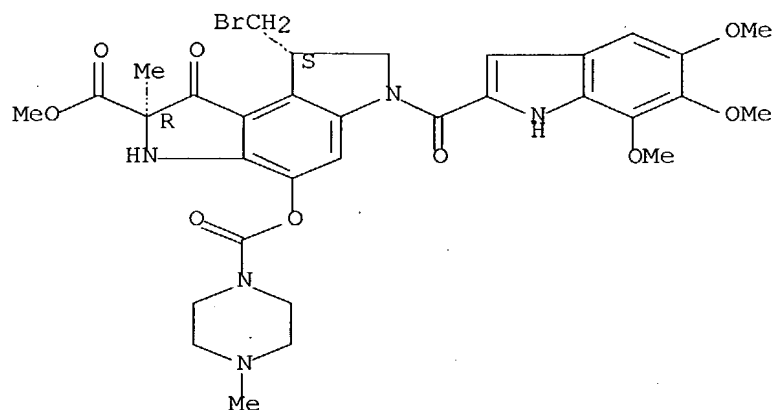
(synthesis, stability and antitumor activity of duocarmycin derivs.)

RN 154901-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[4-methyl-1-
piperazinyl)carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(2R,8S)-

(9CI) (CA INDEX NAME)

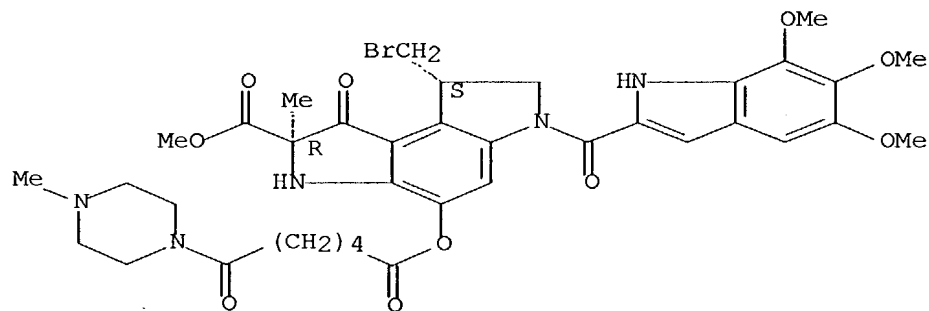
Absolute stereochemistry.



RN 171524-41-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[6-(4-methyl-1-piperazinyl)-1,6-dioxohexyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

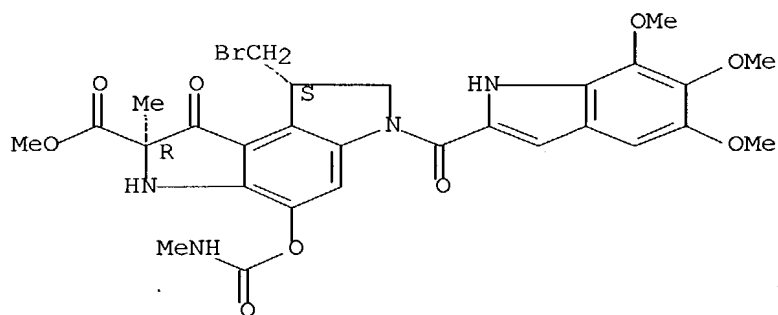
Absolute stereochemistry.



RN 171524-44-0 CAPLUS

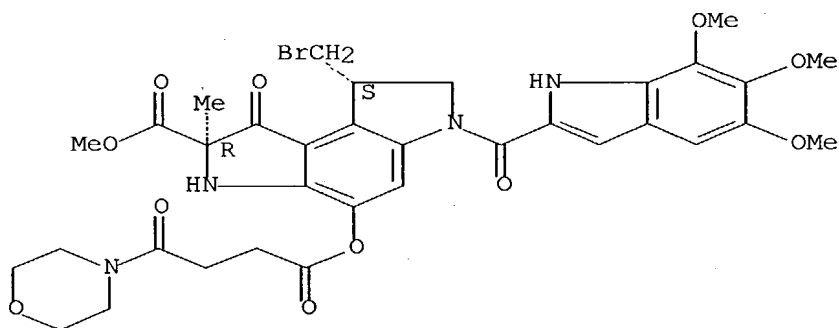
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[6-(4-methyl-1-piperazinyl)-1,6-dioxohexyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



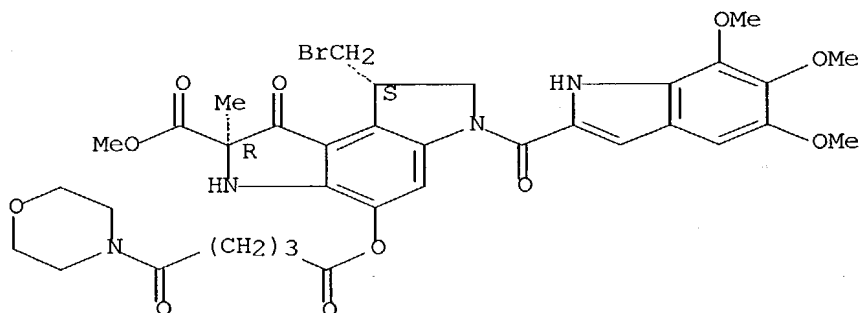
RN 171599-18-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1,4-dioxobutoxy]-1-
 oxo-
 6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 171599-19-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1,5-
 dioxopentyl]oxy]-
 1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
 (2R-trans)- (9CI) (CA INDEX NAME)

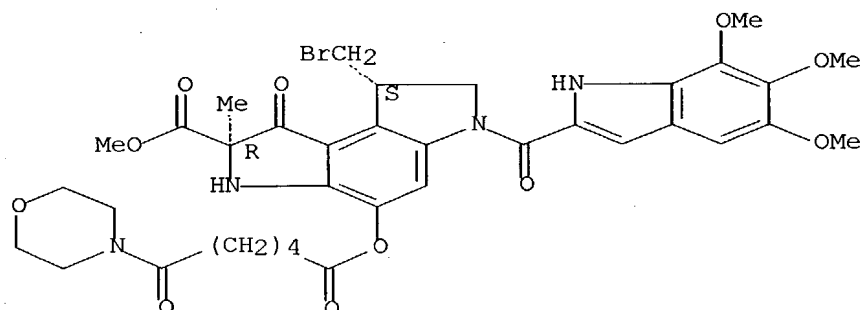
Absolute stereochemistry.



RN 171599-20-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[6-(4-morpholinyl)-1,6-dioxohexyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

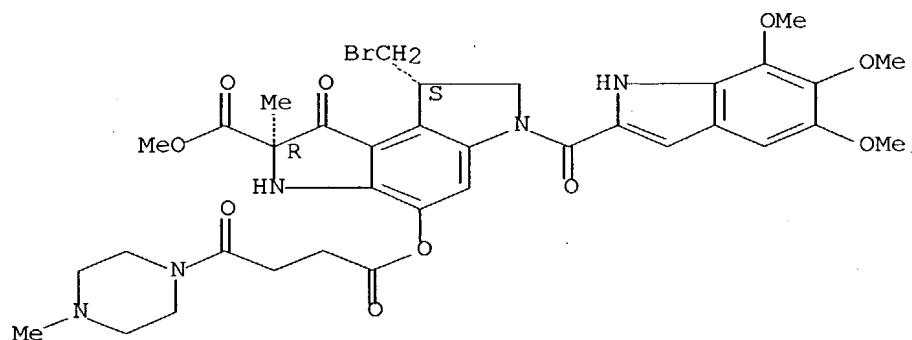
Absolute stereochemistry.



RN 171599-21-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-methyl-1-piperazinyl)-1,4-dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

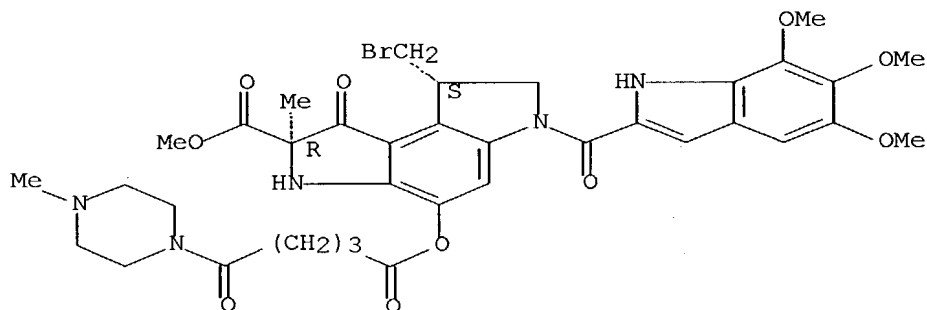
Absolute stereochemistry.



RN 171599-22-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-methyl-1-piperazinyl)-1,5-dioxopentyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

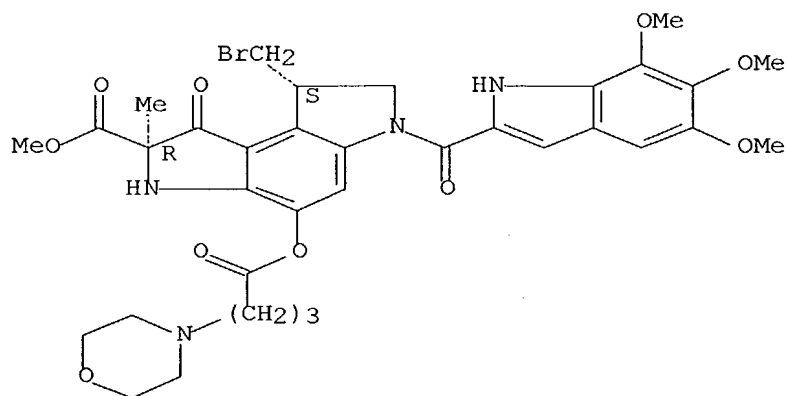
Absolute stereochemistry.



RN 171599-23-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1-oxobutoxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

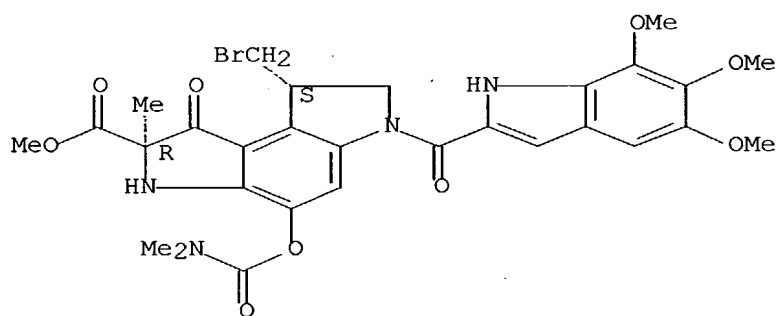


● HCl

RN 171599-25-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
 (9CI) (CA INDEX NAME)

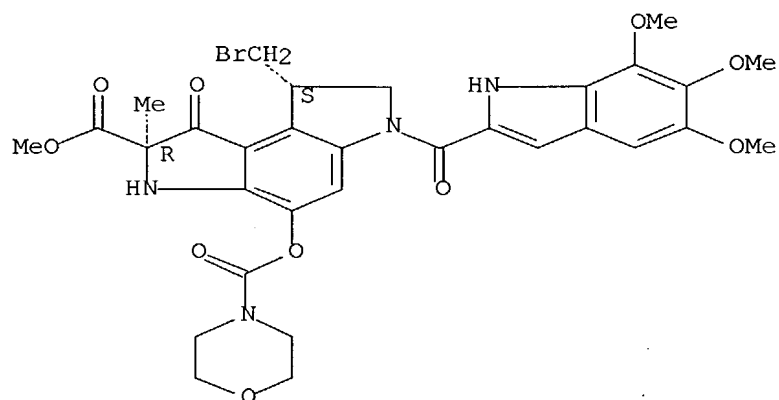
Absolute stereochemistry.



RN 171599-26-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-morpholinylcarbonyl)oxy]-1-oxo-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
 (9CI) (CA INDEX NAME)

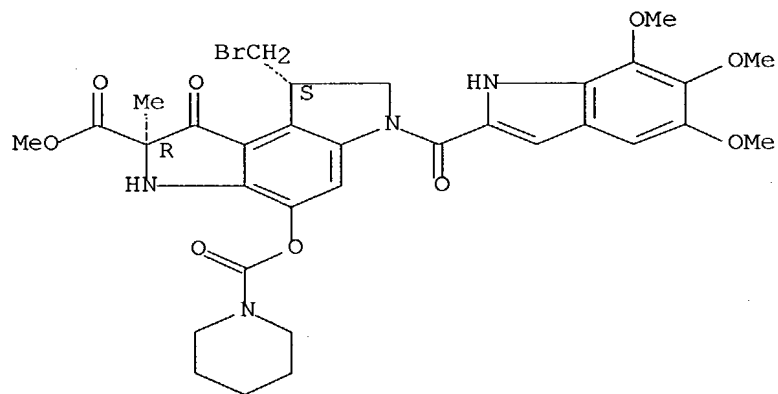
Absolute stereochemistry.



RN 171599-27-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-(9CI) (CA INDEX NAME)

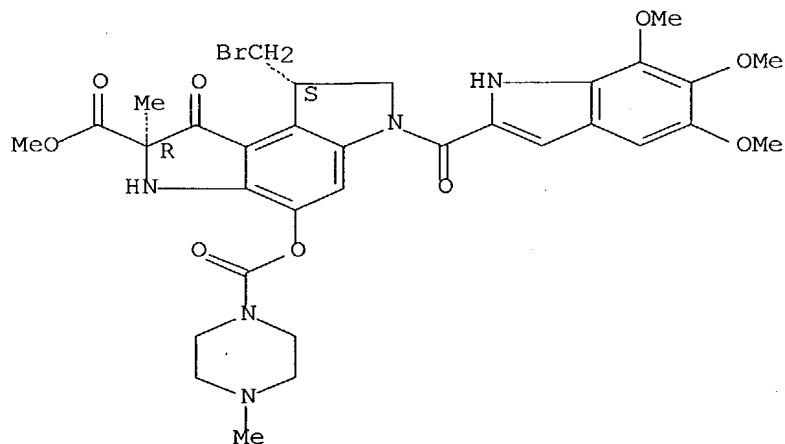
Absolute stereochemistry.



RN 171599-29-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R,8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

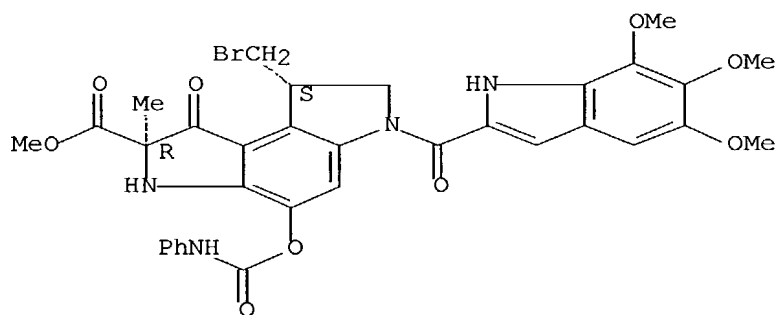


● HCl

RN 171599-30-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[[(phenylamino) carbonyl]oxy]-6-
 [(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (2R-trans)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 124325-94-6, Duocarmycin B2

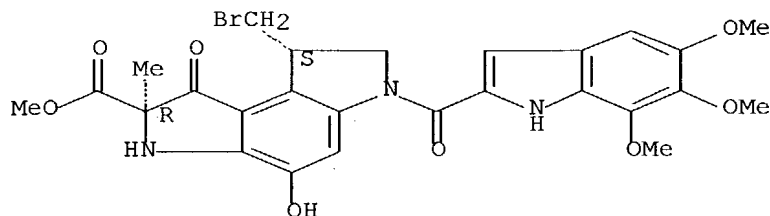
RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); RCT (Reactant); BIOL (Biological study); RACT
 (Reactant or reagent)

(synthesis, stability and antitumor activity of duocarmycin derivs.)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 171524-42-8P 171524-43-9P 171599-24-9P

171599-28-3P

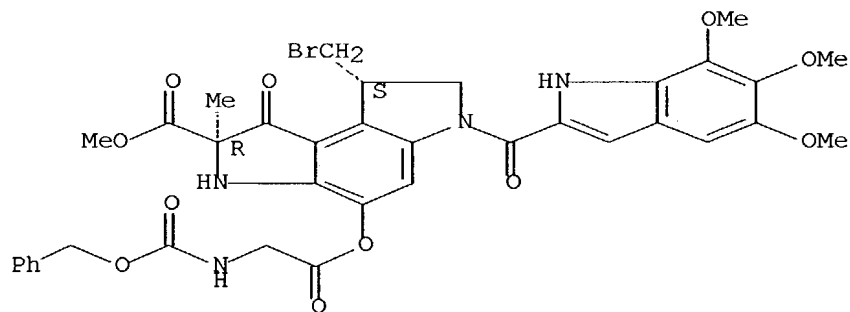
RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis, stability and antitumor activity of duocarmycin derivs.)

RN 171524-42-8 CAPLUS

CN Glycine, N-[(phenylmethoxy)carbonyl]-, 8-(bromomethyl)-1,2,3,6,7,8-
hexahydro-2-(methoxycarbonyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-
2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl ester, (2R-trans)- (9CI)
(CA INDEX NAME)

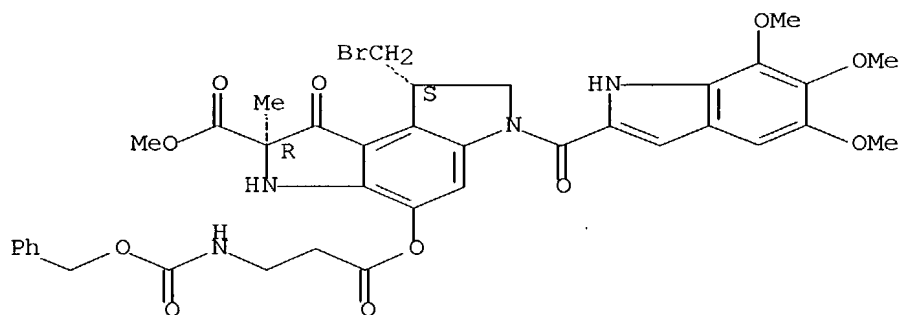
Absolute stereochemistry.



RN 171524-43-9 CAPLUS

CN β -Alanine, N-[(phenylmethoxy)carbonyl]-, 8-(bromomethyl)-1,2,3,6,7,8-
hexahydro-2-(methoxycarbonyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-
2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl ester, (2R-trans)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

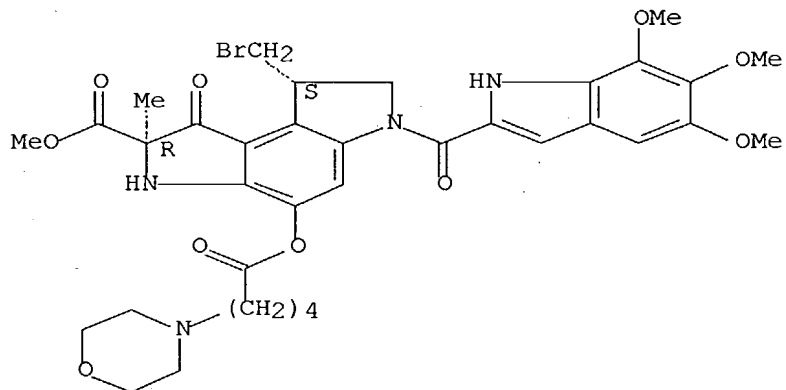


RN 171599-24-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1-oxopentyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



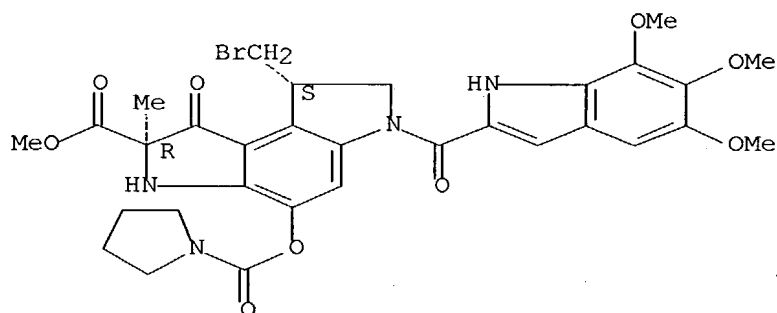
PAGE 2-A

● HCl

RN 171599-28-3 CAPLUS

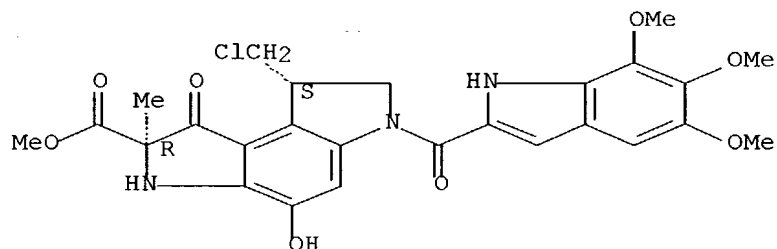
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 77 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:741571 CAPLUS Full-text
 DN 123:285601
 TI Duocarmycins, potent antitumor antibiotics produced by *Streptomyces* sp. structures and chemistry
 AU Yasuzawa, Tohru; Muroi, Ken'ichi; Ichimura, Michio; Takahashi, Isami; Ogawa, Tatsuhiko; Takahashi, Keiichi; Sano, Hiroshi; Saitoh, Yutaka
 CS Tokyo Res. Lab., Tokyo, 194, Japan
 SO Chemical & Pharmaceutical Bulletin (1995), 43(3), 378-91
 CODEN: CPBTAL; ISSN: 0009-2363
 PB Pharmaceutical Society of Japan
 DT Journal
 LA English
 AB Seven novel potent antitumor antibiotics, duocarmycins A, C1, C2, D, B1, B2 and SA, were isolated from three independently collected *Streptomyces* sp. The complete structures, including absolute stereochem., were determined by spectral and chemical studies of those duocarmycins and several derivs. Duocarmycins A and SA possess a 1,2,7,7a-tetrahydrocycloprop[1,2-c]indol-4-one subunit, a common pharmacophore with that of CC-1065 found from *Streptomyces zelensis*.
 IT **118292-36-7**, Duocarmycin C2
 RL: PRP (Properties)
 (isolation and structures of seven duocarmycins, potent antitumor antibiotics produced by *Streptomyces* sp.)
 RN 118292-36-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



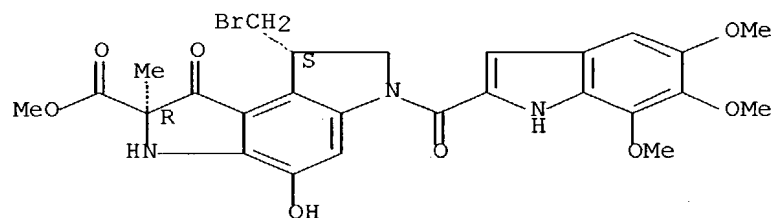
IT 124325-94-6, Duocarmycin B2

RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(isolation and structures of seven duocarmycins, potent antitumor antibiotics produced by Streptomyces sp.)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 129953-18-0P 168776-87-2P 169102-68-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

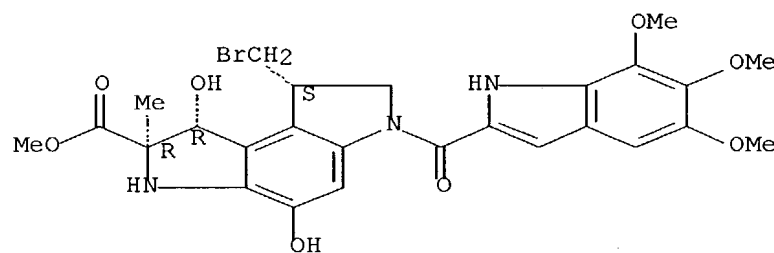
(Reactant or reagent)

(isolation and structures of seven duocarmycins, potent antitumor antibiotics produced by Streptomyces sp.)

RN 129953-18-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1,4-dihydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1 α ,2 β ,8 α)]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



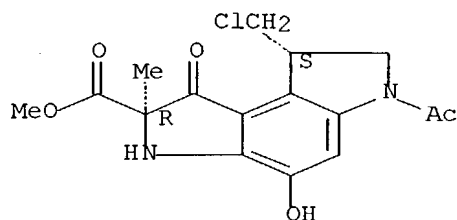
RN 168776-87-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-8-(chloromethyl)-

1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester, (2R-trans)-

(9CI) (CA INDEX NAME)

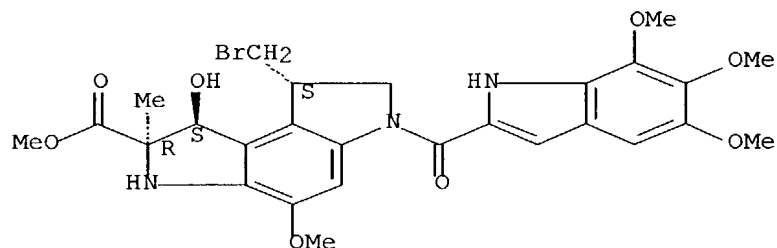
Absolute stereochemistry. Rotation (-).



RN 169102-68-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-
1H-indol-2-yl)carbonyl]-, methyl ester, [2R-(2 α ,3 α ,4 β)]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



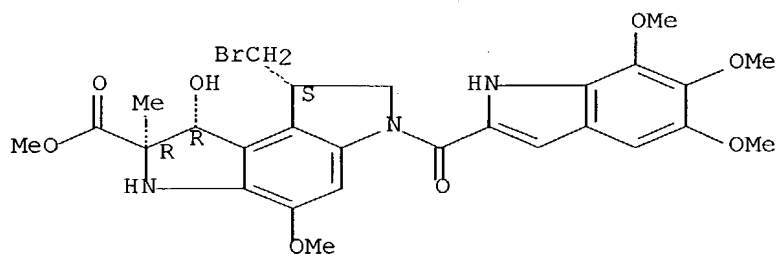
IT 129953-21-5P 168776-83-8P 168776-84-9P
168776-85-0P 168776-86-1P 168776-88-3P
168960-56-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(isolation and structures of seven duocarmycins, potent antitumor
antibiotics produced by Streptomyces sp.)

RN 129953-21-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-
1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1 α ,2 β ,8 α)]-
(9CI) (CA INDEX NAME)

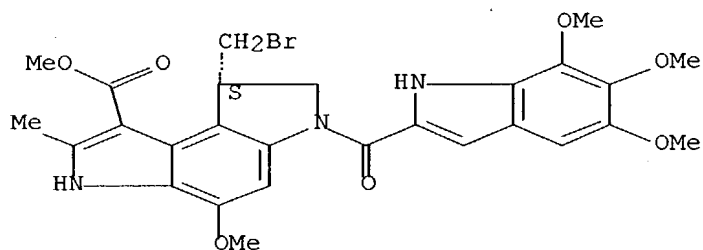
Absolute stereochemistry. Rotation (-).



RN 168776-83-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

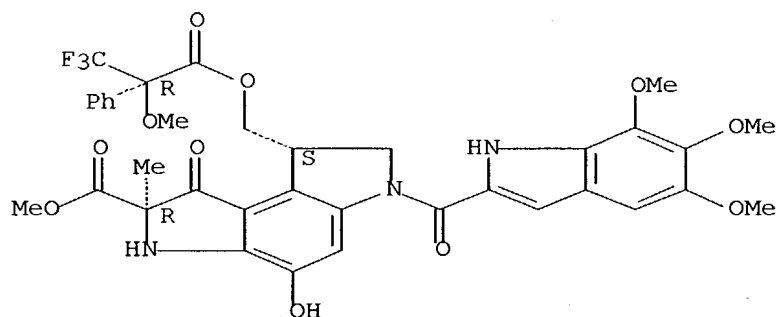
Absolute stereochemistry. Rotation (-).



RN 168776-84-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-8-[(3,3,3-trifluoro-2-methoxy-1-oxo-2-phenylpropoxy)methyl]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [2R-[2α,8β(R*)]]- (9CI) (CA INDEX NAME)

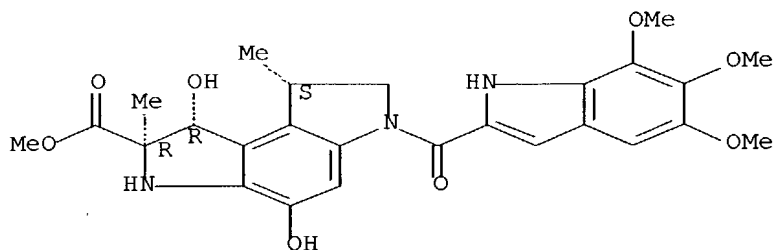
Absolute stereochemistry. Rotation (+).



RN 168776-85-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-1,4-dihydroxy-2,8-dimethyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1 α ,2 β ,8 α)]- (9CI) (CA INDEX NAME)

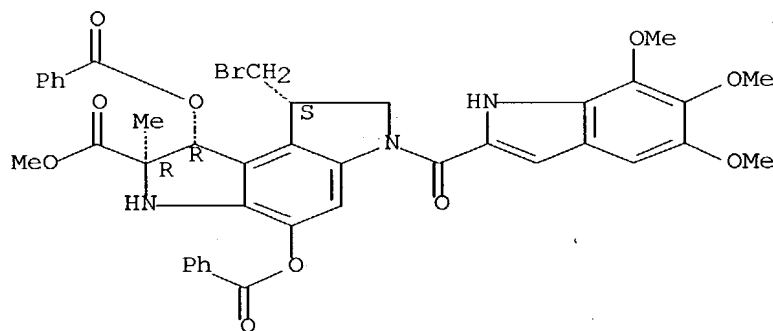
Absolute stereochemistry. Rotation (-).



RN 168776-86-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,4-bis(benzoyloxy)-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1 α ,2 β ,8 α)]- (9CI) (CA INDEX NAME)

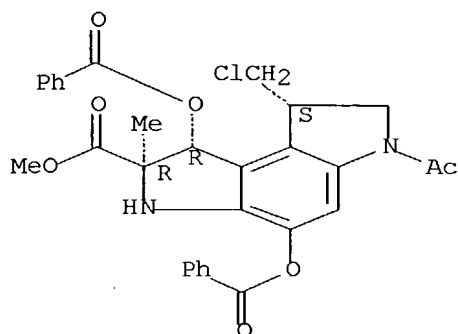
Absolute stereochemistry. Rotation (-).



RN 168776-88-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-1,4-bis(benzoyloxy)-8-(chloromethyl)-1,2,3,6,7,8-hexahydro-2-methyl-, methyl ester, [1R-(1 α ,2 β ,8 α)]- (9CI) (CA INDEX NAME)

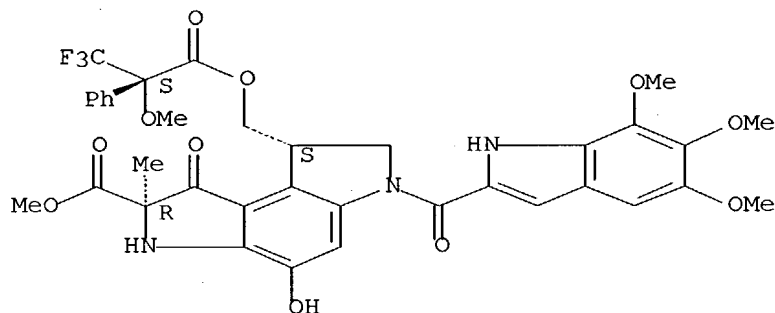
Absolute stereochemistry. Rotation (-).



RN 168960-56-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-8-[(3,3,3-trifluoro-2-methoxy-1-oxo-2-phenylpropoxy)methyl]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [2R-[2 α ,8 β (S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 78 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN.

AN 1995:389254 CAPLUS Full-text

DN 122:177884

TI Intracellular carboxyl esterase activity is a determinant of cellular sensitivity to the antineoplastic agent KW-2189 in cell lines resistant to

cisplatin and CPT-11

AU Ogasawara, Hayato; Nishio, Kazuto; Kanzawa, Fumihiko; Lee, Yong-Sik; Funayama, Yasunori; Ohira, Tatsuo; Kuraishi, Yasunobu; Isogai, Yukihide; Saijo, Nagahiro

CS Pharmacology Div., National Cancer Center Res. Inst., Tokyo, 104, Japan

SO Japanese Journal of Cancer Research (1995), 86(1), 124-9

CODEN: JJCREP; ISSN: 0910-5050

PB Japanese Cancer Association

DT Journal

LA English

AB KW-2189, a novel antitumor antibiotic belonging to the duocarmycins, possesses marked DNA-binding activity upon activation by carboxyl esterase to its active form, DU-86. Three duocarmycins, KW-2189, DU-86 and duocarmycin SA, were active against the cisplatin (CDDP)-resistant human non-small cell lung cancer cell lines PC-9/CDDP and PC-14/CDDP, and the multidrug-resistant human small cell lung cancer cell line H69/VP. However, HAC2/0.1, a CDDP-resistant human ovarian cancer cell line which is also resistant to CPT-11 because of decreased intracellular activation of CPT-11, was about 12.8-fold more resistant to KW-2189. HAC2/0.1 was not resistant to other duocarmycins as compared to its parental cell line, HAC2. There was no difference between HAC2 and HAC2/0.1 with regard to the intracellular accumulation of KW-2189. Addition of 130 mU/mL of carboxyl esterase to the culture medium did not influence the sensitivity of HAC2 cells to KW-2189. However, the sensitivity of HAC2/0.1 cells to KW-2189 was enhanced to the level of HAC2. These results suggest that HAC2/0.1 is less potent than HAC2 in activating KW-2189. The carboxyl esterase activity of whole-cell and microsomal exts. from HAC2/0.1 was approx. 60% of that from HAC2. The cell-free experiment revealed that KW-2189 bound to DNA more efficiently in the presence of HAC2 than HAC2/0.1 cell extract. It was concluded that decreased intracellular carboxyl esterase activity in HAC2/0.1 cells caused decreased intracellular conversion of KW-2189 to its active form, thus producing resistance to KW-2189. The decreased conversion of CPT-11 to SN-38 in HAC2/0.1 cells might be explained by decreased carboxyl esterase activity.

IT 154889-68-6, KW-2189

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES

(Uses)

(intracellular carboxyl esterase activity as determinant of cellular sensitivity to the antineoplastic agent KW-2189 in cell lines resistant to cisplatin and CPT-11)

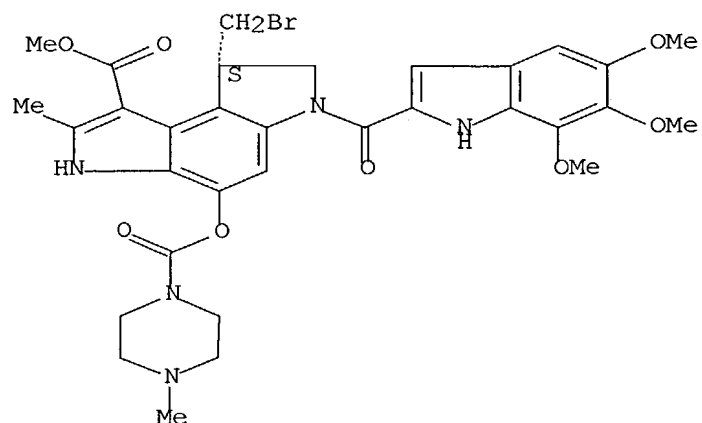
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



L10 ANSWER 79 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:347075 CAPLUS Full-text

DN 122:132847

TI Method for preparation of duocarmycin derivatives with antitumor activity

IN Kinugawa, Masahiko; Sakaguchi, Akihiko; Ogasa, Takehiro; Saito, Hiromitsu;

Nagamura, Akihito; Tomioka, Shinji

PA Kyowa Hakko Kogyo Kk, Japan

SO Jpn. Kokai Tokkyo Koho, 11 pp.

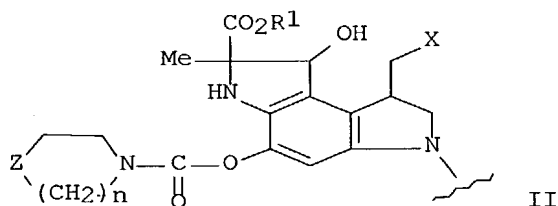
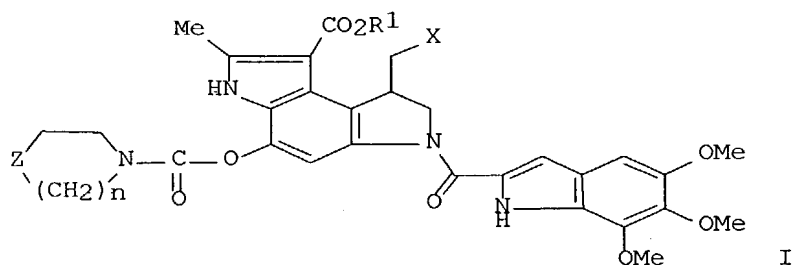
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	JP 06298762	A2	19941025	JP 1993-85943	19930413
PRAI	JP 1993-85943		19930413		
OS	CASREACT 122:132847; MARPAT 122:132847				
GI					



AB The title compds. (I; R1 = lower alkyl, allyl, CH2Ph; X = Cl, Br; Z = CH2, O, NR2; wherein R2 = H, lower alkyl; n = 1-4), useful as antitumor agents (no data), are prepared by treating 1,2,3,4-tetrahydro-3H-pyrrolo[3,2-e]indole-7-carboxylic acid derivative (II; R1, X, Z, n = same as above). Thus, Me (1S,7R)-1-bromomethyl-7-methyl-5-[(4-methylpiperazinyl)carbonyloxy]-8-oxo-3-[(5,6,7-trimethoxyindol-2-yl)carbonyl]-1,2,7,8-tetrahydro-3H-pyrrolo[3,2-e]indole-7-carboxylate was reduced by NaBH4 in allyl alc. to give, after silica gel chromatog., 63% intermediate II (R1 = Me, X = Br, Z = MeN, n = 2). The latter compound was stirred with MeSO3H in CH2Cl2 at 47-53° for 5 h to give 86.3% title compound I (R1 = Me, X = Br, Z = MeN, n = 2).

IT **124325-94-6**

RL: RCT (Reactant); RACT (Reactant or reagent)

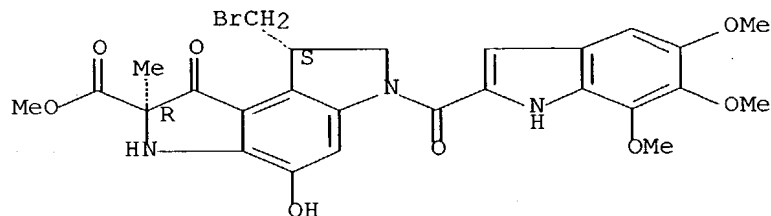
(esterification with N-methylpiperazinylcarbonyl chloride hydrochloride

in preparation of duocarmycin derivs. with antitumor activity)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 160819-29-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and dehydration in preparation of duocarmycin derivs.

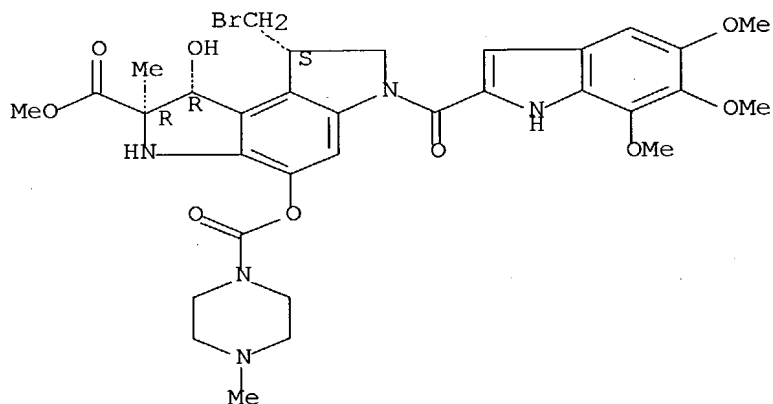
with antitumor

activity)

RN 160819-29-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[(4-methyl-1-
piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154901-65-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

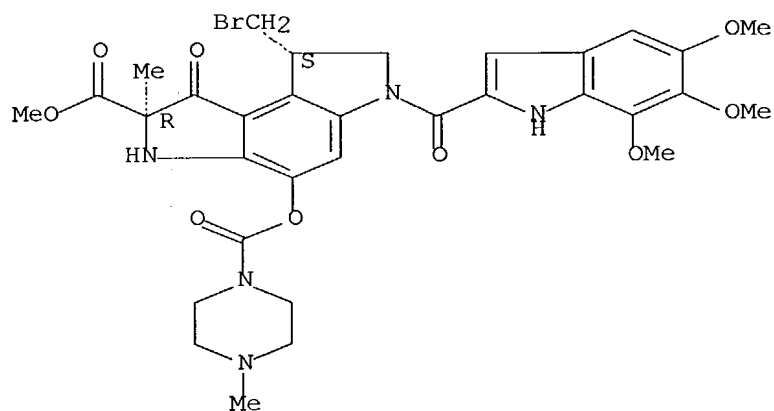
(preparation and reduction with sodium borohydride in preparation of
duocarmycin

derivs. with antitumor activity)

RN 154901-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-
piperazinyl)carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 154889-68-6P 160819-28-3P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of duocarmycin derivs. with antitumor activity by
acid-catalyzed dehydration of
hydroxytetrahydropyrroloindolecarboxylic
acid derivative)

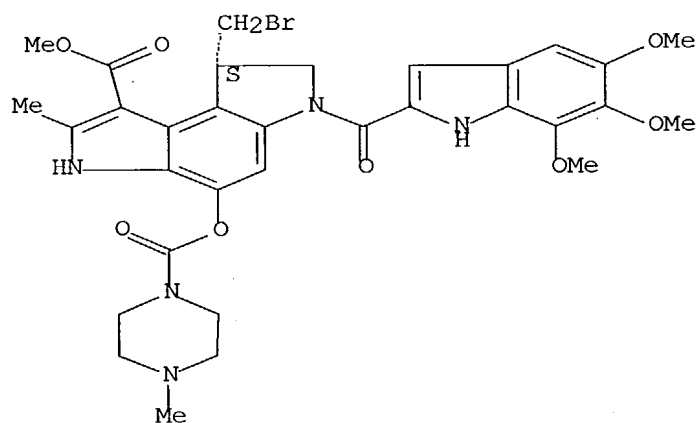
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.

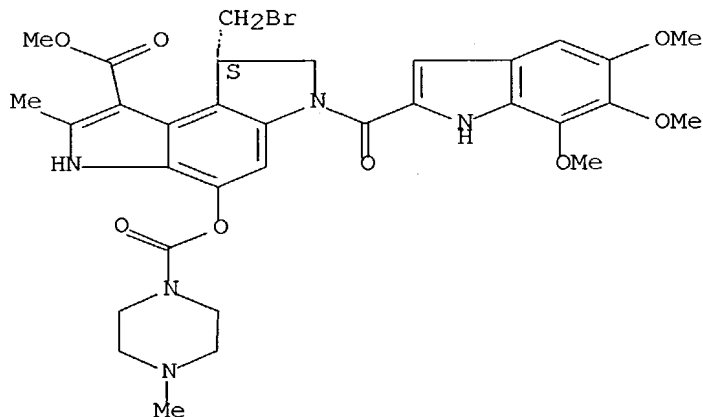


RN 160819-28-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,
(8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



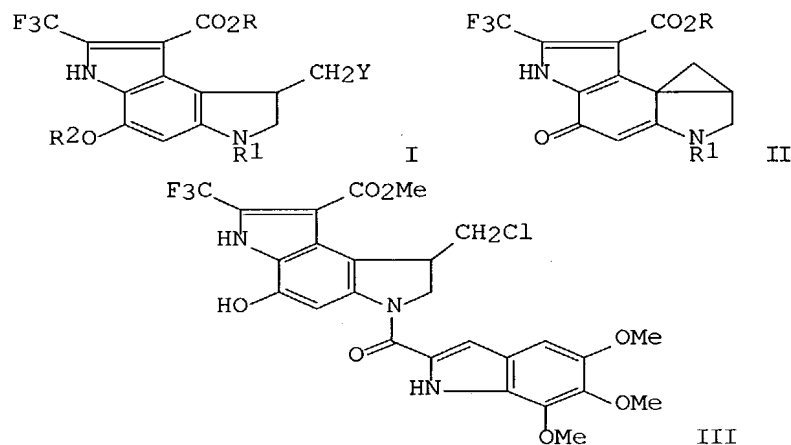
PAGE 2-A

● HBr

L10 ANSWER 80 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:605331 CAPLUS Full-text
DN 121:205331
TI preparation of (trifluoromethyl)pyrroloindolecarboxylic esters as
antitumor agents
IN Terashima, Shiro; Fukuda, Yasumichi; Oomori, Yasuo
PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center
SO PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9404535	A1	19940303	WO 1993-JP1159	19930819
	W:	AU, BB, BG, BR, CA, CZ, FI, HU, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US			
	RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	JP 06116269	A2	19940426	JP 1993-204255	19930818
	JP 3514490	B2	20040331		

EP 656360	A1	19950607	EP 1994-908108	19930819
EP 656360	B1	20021120		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 71493	A2	19951128	HU 1995-494	19930819
AU 689443	B2	19980402	AU 1993-47618	19930819
AU 9347618	A1	19940315		
CA 2142869	C	20020101	CA 1993-2142869	19930819
AT 228132	E	20021215	AT 1994-908108	19930819
PT 656360	T	20030228	PT 1994-94908108	19930819
ES 2188608	T3	20030701	ES 1994-908108	19930819
TW 394774	B	20000621	TW 1993-82108171	19931004
US 5629430	A	19970513	US 1995-381981	19950614
PRAI JP 1992-222862	A	19920821		
JP 1993-204255	A	19930818		
WO 1993-JP1159	W	19930819		
OS MARPAT 121:205331				
GI				



AB The title compds. [I, II; R = alkyl; R1 = α -amino acid residue, etc.; R2 = H, protecting group; Y = halo, arylsulfonyloxy, etc.] are prepared I (R = Me, R1 = Me3CO2C, R2 = H, Y = Cl) was added to 3M HCl-EtOAc with stirring at room temperature, the residue after distillation was treated with 5,6,7-trimethoxyindole-2-carboxylic acid and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl in DMF with stirring at room temperature under Ar to give 82% III, which showed IC50 of 0.24 ng/mL against P-388 mouse leukemic cells. Also prepared and tested were 103 addnl. I and II.

IT **194093-62-4P 194093-63-5P 194093-64-6P 194093-65-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

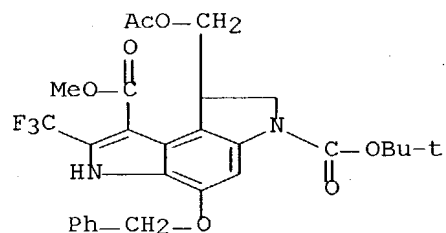
RACT

(Reactant or reagent)

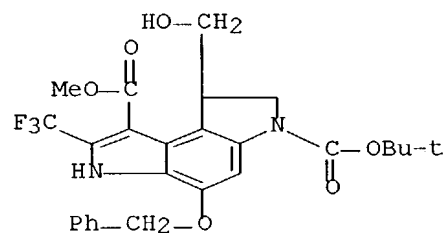
(preparation and reaction of, in preparation of antitumor agents)

RN 194093-62-4 CAPLUS

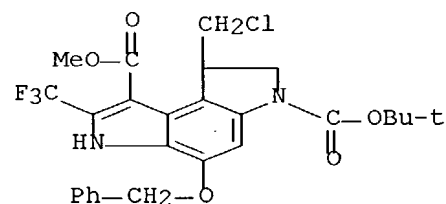
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-63-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-,
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

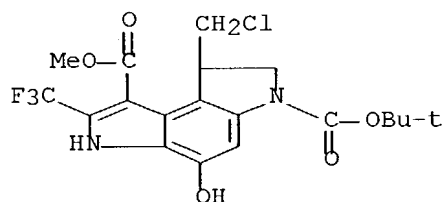


RN 194093-64-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-65-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,

8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



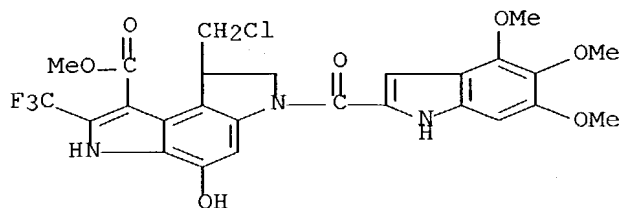
IT 157822-64-5P 157822-68-9P 157822-69-0P
157822-70-3P 157822-71-4P 157822-72-5P
157822-73-6P 157822-74-7P 157822-75-8P
157822-76-9P 157822-91-8P 157822-92-9P
157822-93-0P 157822-94-1P 157822-95-2P
157822-96-3P 157822-97-4P 157822-98-5P
157822-99-6P 157823-00-2P 157823-01-3P
157823-02-4P 157823-03-5P 157823-04-6P
157823-05-7P 157823-06-8P 157823-07-9P
157823-08-0P 157823-09-1P 157823-10-4P
157823-11-5P 157823-12-6P 157823-13-7P
157823-14-8P 157823-15-9P 157823-16-0P
157823-17-1P 157823-18-2P 157823-19-3P
157823-20-6P 157823-21-7P 157823-22-8P
157823-23-9P 157823-24-0P 157823-25-1P
157823-26-2P 157823-27-3P 157823-28-4P
157823-29-5P 157823-30-8P 157823-31-9P
157823-39-7P 157823-40-0P 157823-41-1P
157823-42-2P 157823-43-3P 157823-44-4P
157823-45-5P 157823-46-6P 157823-47-7P
157823-48-8P 157823-49-9P 157823-50-2P
157823-51-3P 157823-52-4P 157823-53-5P
157823-54-6P 157823-55-7P 157823-56-8P
157904-26-2P 157904-27-3P 157904-28-4P
157904-29-5P 157904-30-8P 157904-31-9P
157904-32-0P 157904-33-1P 157904-34-2P
194093-65-7P 194093-68-0P 194093-70-4P
194093-71-5P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);

BIOL (Biological study); PREP (Preparation); USES (Uses).
(preparation of, as antitumor agent)

RN 157822-64-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
2-
tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(4,5,6-trimethoxy-1H-indol-
yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

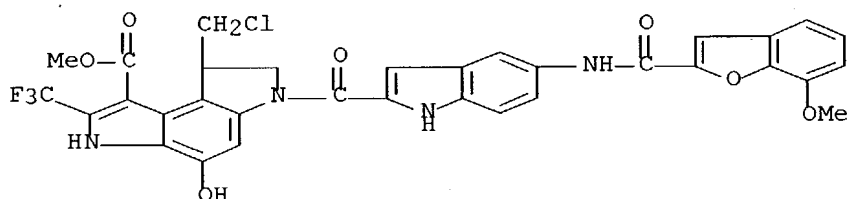


RN 157822-68-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

1H-tetrahydro-4-hydroxy-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-

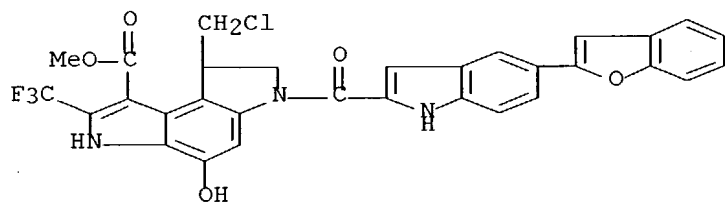
indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157822-69-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-(2-benzofuranyl)-1H-

indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



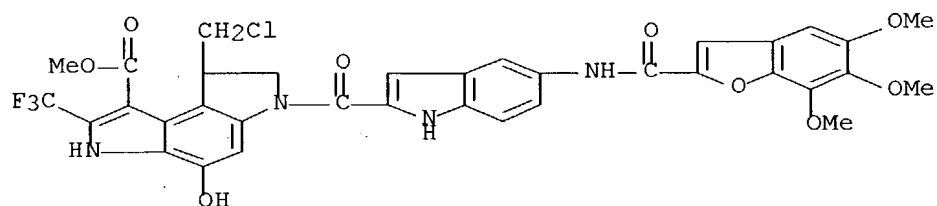
RN 157822-70-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester

(9CI)

(CA INDEX NAME)



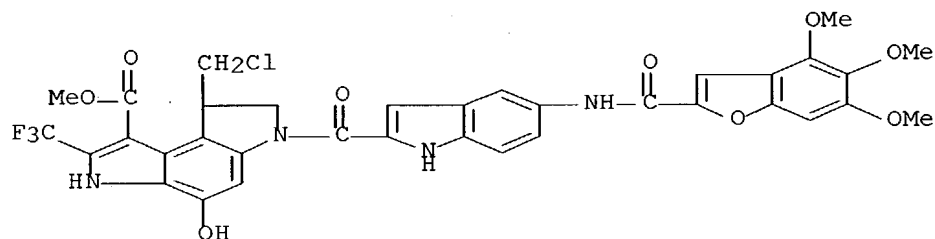
RN 157822-71-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[4,5,6-trimethoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester

(9CI)

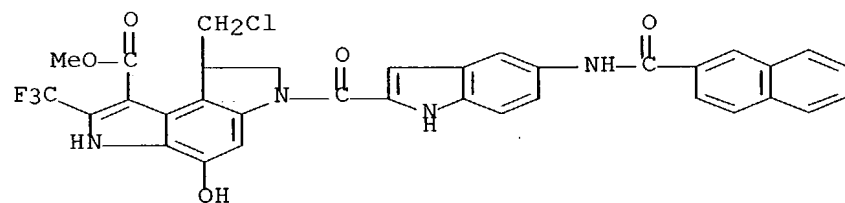
(CA INDEX NAME)



RN 157822-72-5 CAPLUS

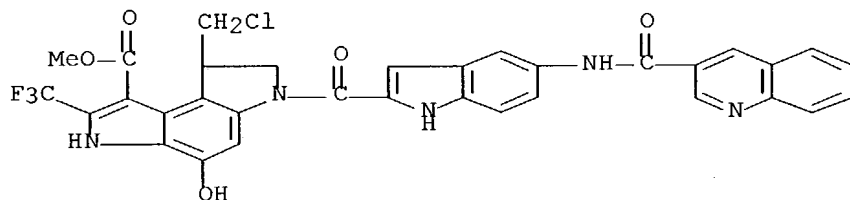
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-6-[[5-[(2-naphthalenylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)

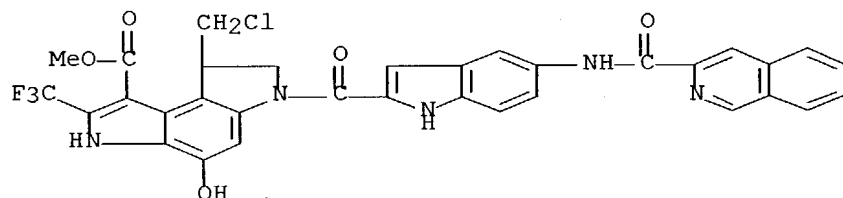


RN 157822-73-6 CAPLUS

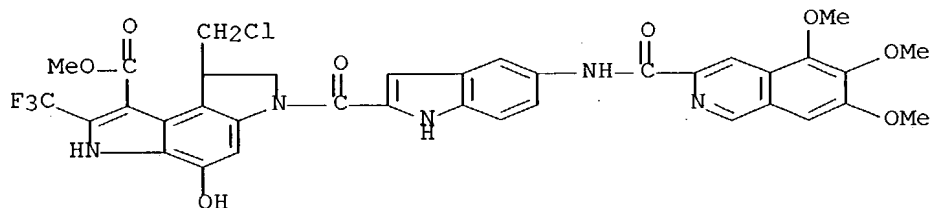
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[(3-quinolinylcarbonyl)amino]-1H-indol-2-
yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157822-74-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-
yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157822-75-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-3-
isoquinolinyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester
(9CI)
(CA INDEX NAME)

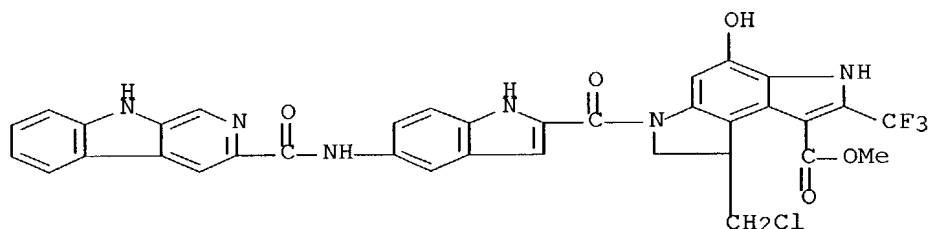


RN 157822-76-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

1H-tetrahydro-4-hydroxy-6-[[5-[(9H-pyrido[3,4-b]indol-3-ylcarbonyl)amino]-

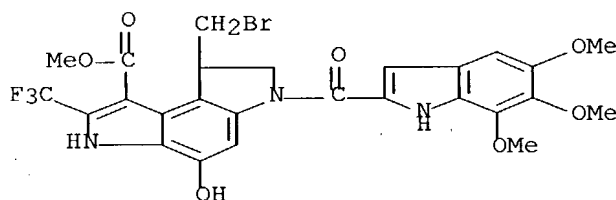
indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157822-91-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-

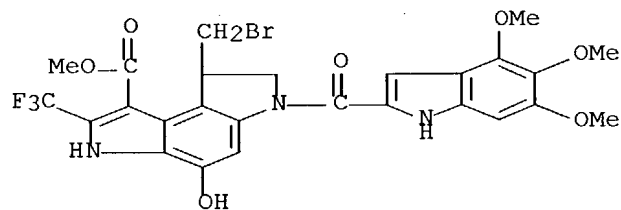
2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



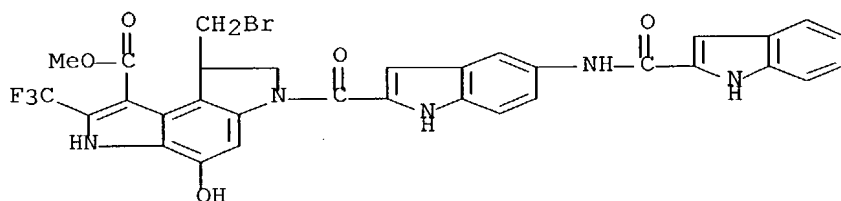
RN 157822-92-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(4,5,6-trimethoxy-1H-indol-

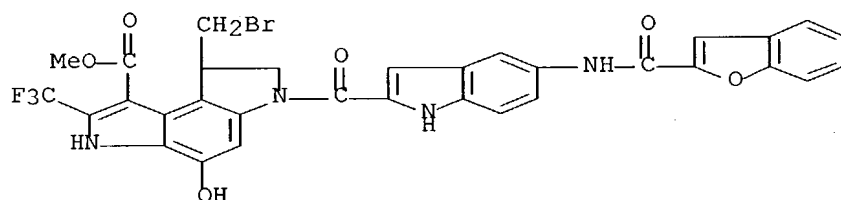
2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



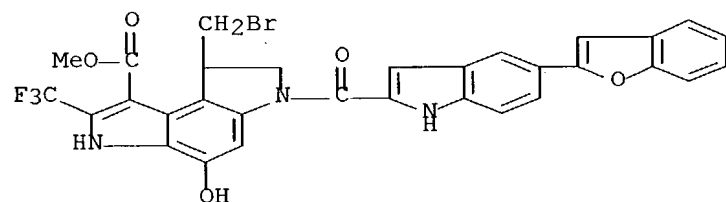
RN 157822-93-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157822-94-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI)
 (CA INDEX NAME)

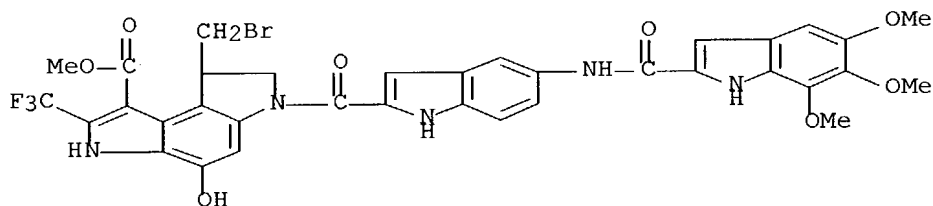


RN 157822-95-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-(2-benzofuranyl)-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



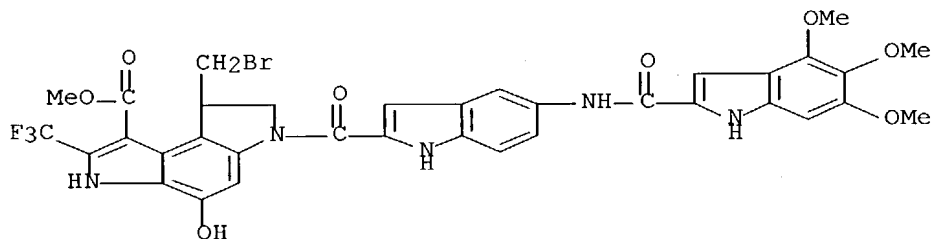
RN 157822-96-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI)
(CA INDEX NAME)



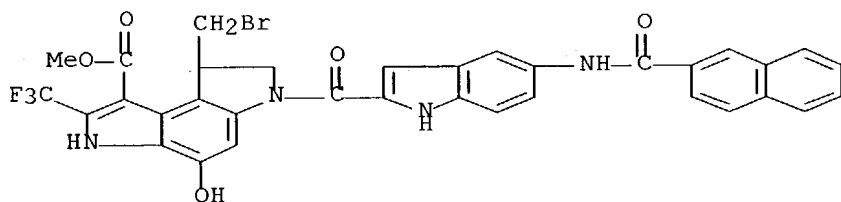
RN 157822-97-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[4,5,6-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI)
(CA INDEX NAME)



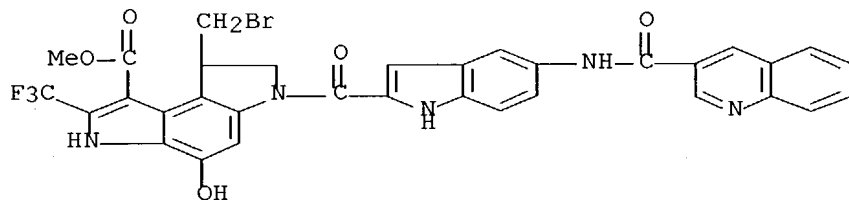
RN 157822-98-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(2-naphthalenylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



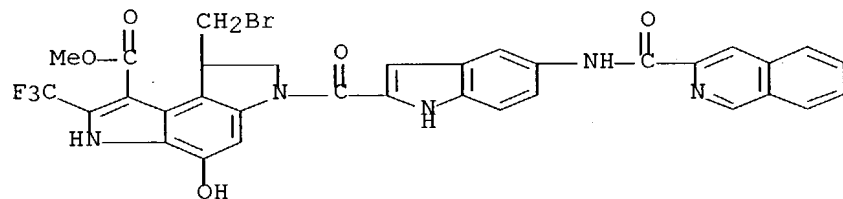
RN 157822-99-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(3-quinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157823-00-2 CAPLUS

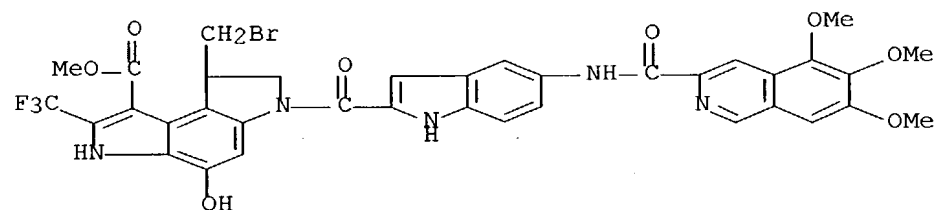
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 157823-01-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-3-isoquinolinyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI)

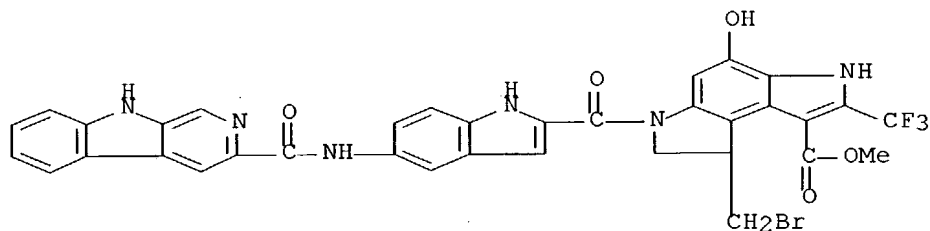
(CA INDEX NAME)



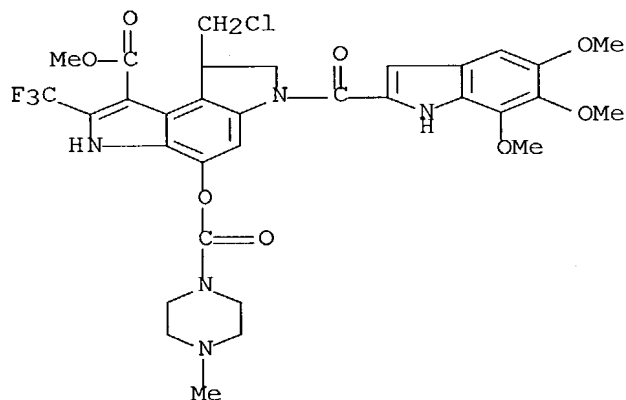
RN 157823-02-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

1H- tetrahydro-4-hydroxy-6-[[5-[(9H-pyrido[3,4-b]indol-3-ylcarbonyl)amino]-
indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX
NAME)

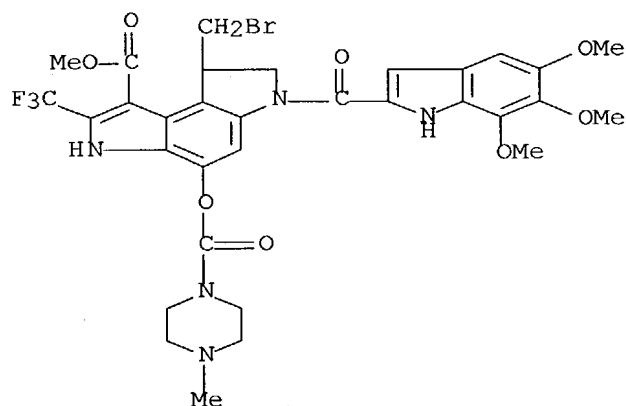


RN 157823-03-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-2-
(trifluoromethyl)-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

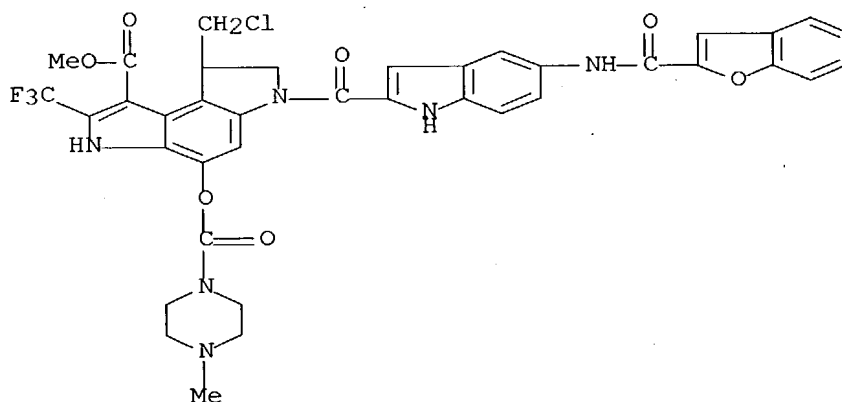
RN 157823-04-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-2-
(trifluoromethyl)-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 157823-05-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



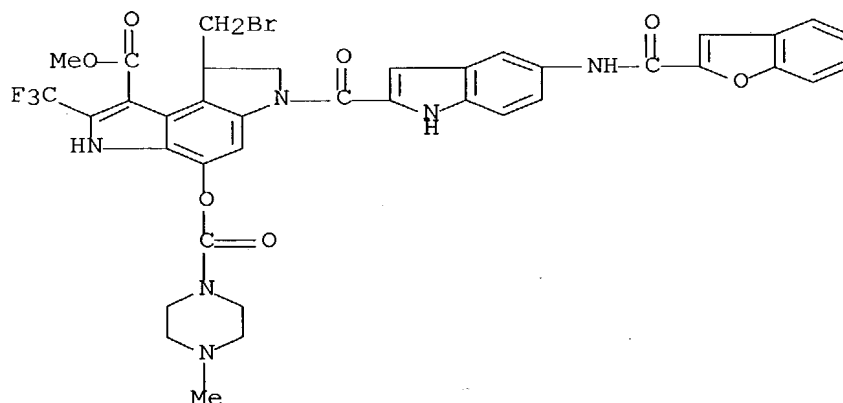
PAGE 2-A

● HCl

RN 157823-06-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

NAME)

PAGE 1-A



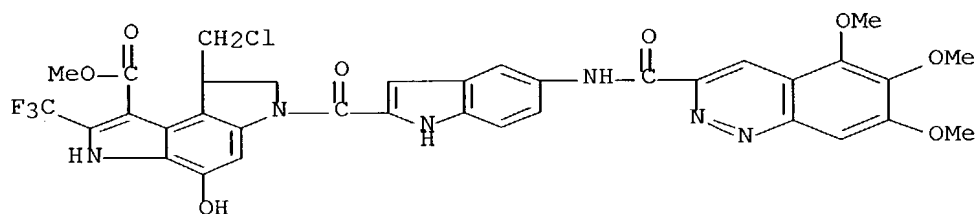
PAGE 2-A

● HCl

RN 157823-07-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

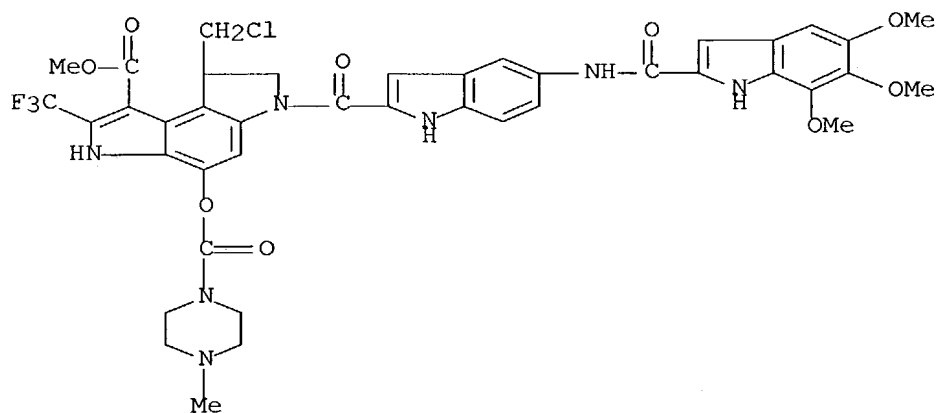
tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-3-cinnolinyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI)
(CA INDEX NAME)



RN 157823-08-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-
[[5-[[5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

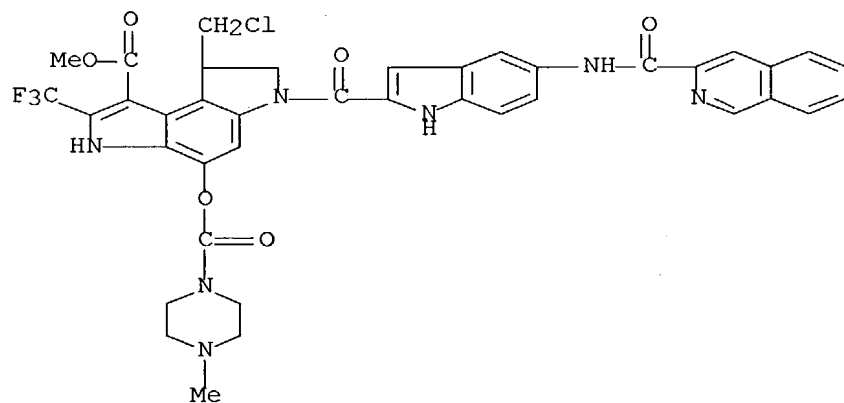


RN 157823-09-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-

4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)

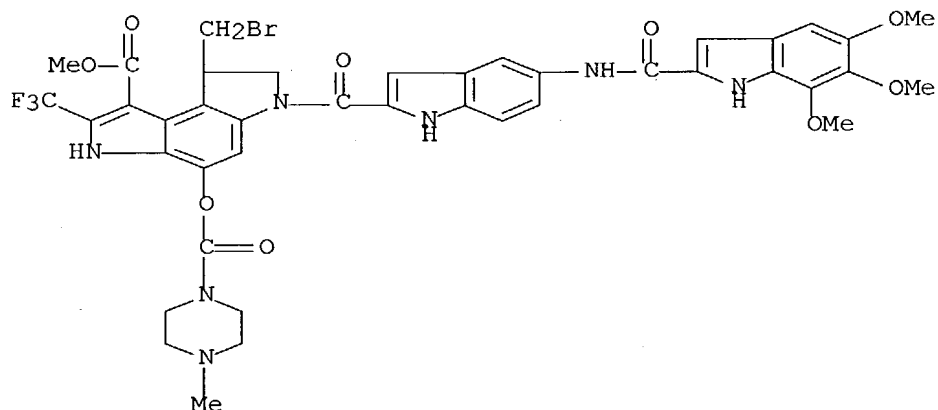


RN 157823-10-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-

(trifluoromethyl)-6-

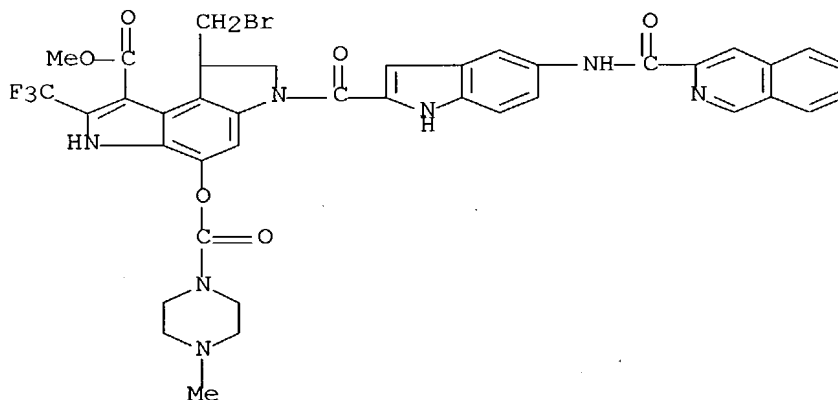
[[5-[[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 157823-11-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



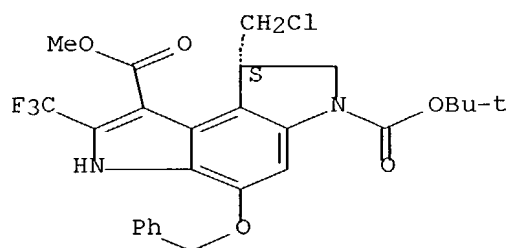
PAGE 2-A

● HCl

RN 157823-12-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

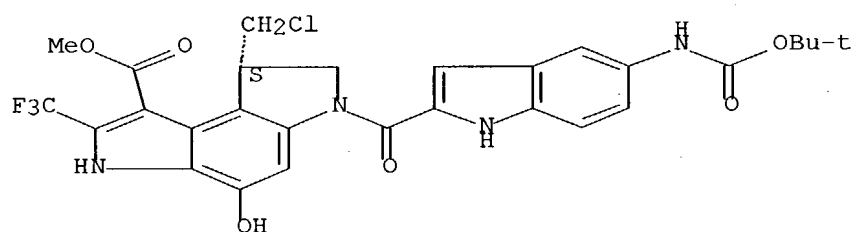
Absolute stereochemistry. Rotation (-).



RN 157823-13-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[(1,1-dimethylethoxy) carbonyl] amino]-1H-indol-2-yl] carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

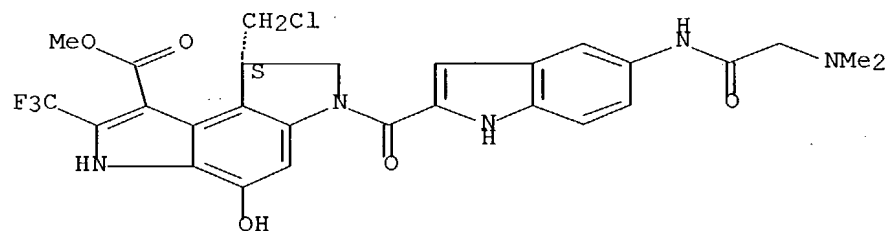
Absolute stereochemistry.



RN 157823-14-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[2-(dimethylamino) acetyl] amino]-1H-indol-2-yl] carbonyl]-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

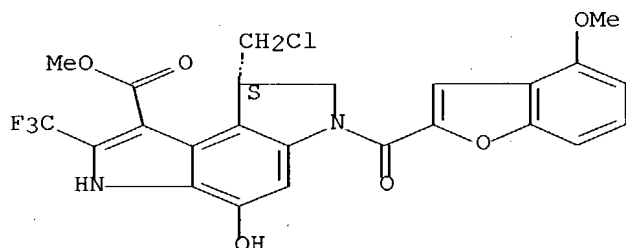
Absolute stereochemistry.



RN 157823-15-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(4-methoxy-2-benzofuranyl)carbonyl]-2-
(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

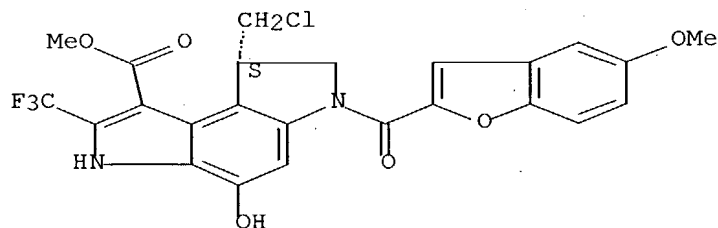
Absolute stereochemistry.



RN 157823-16-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-
(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

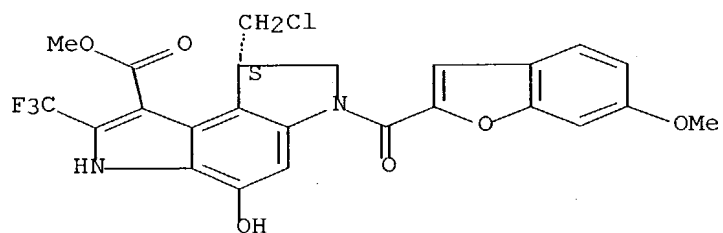
Absolute stereochemistry.



RN 157823-17-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[(6-methoxy-2-benzofuranyl)carbonyl]-2-
(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

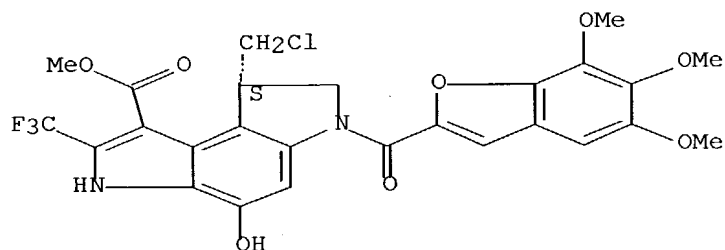
Absolute stereochemistry.



RN 157823-18-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

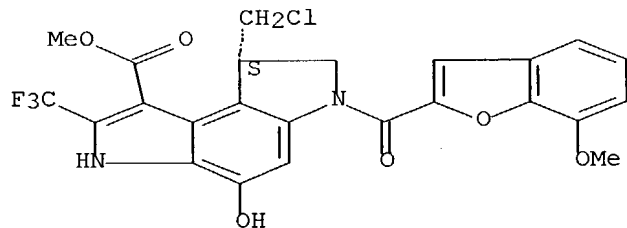
Absolute stereochemistry. Rotation (+).



RN 157823-19-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(7-methoxy-2-benzofuranyl)carbonyl]-2-(trifluoromethyl)-, methyl ester, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

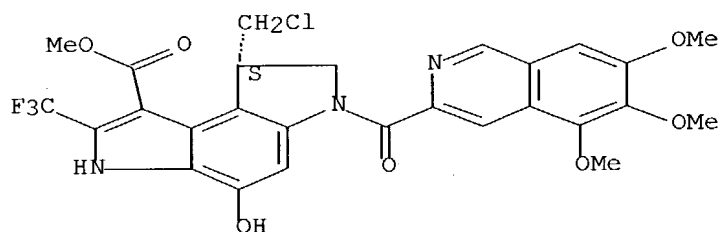


RN 157823-20-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-3-isoquinolinyl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

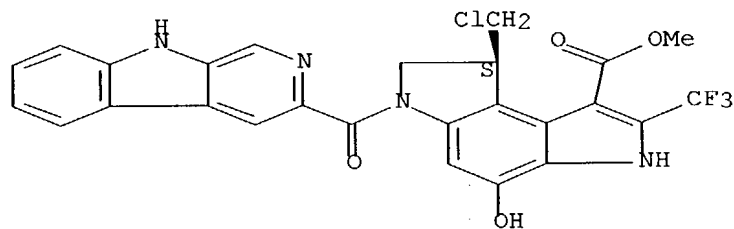
Absolute stereochemistry.



RN 157823-21-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-(9H-pyrido[3,4-b]indol-3-ylcarbonyl)-2-(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

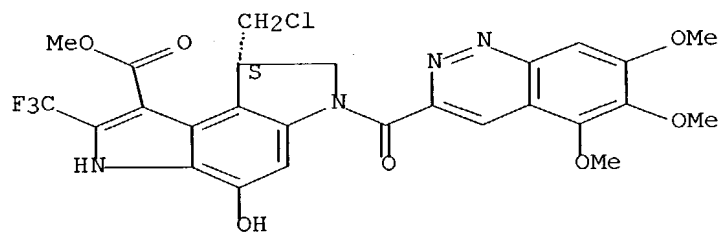
Absolute stereochemistry.



RN 157823-22-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-3-cinnolinyl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

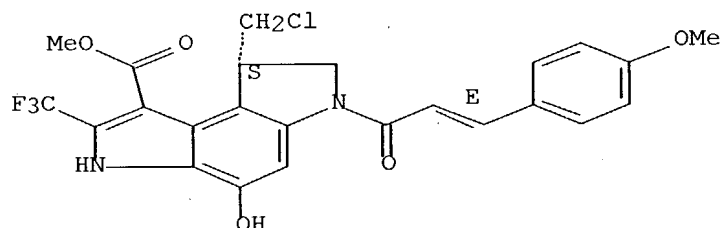


RN 157823-23-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-
(trifluoromethyl)-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

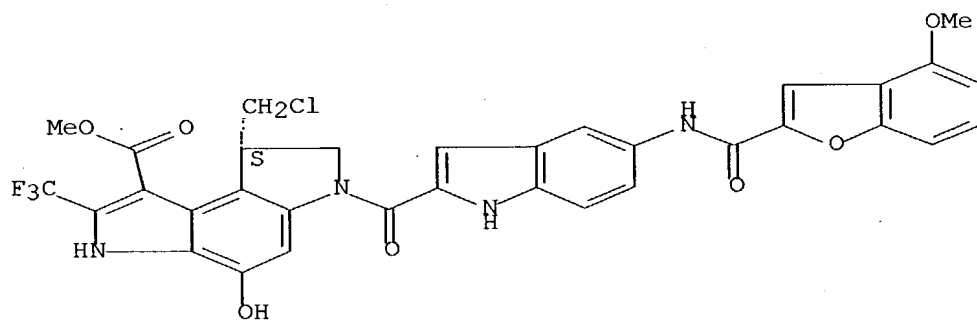
Double bond geometry as shown.



RN 157823-24-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[[[4-methoxy-2-benzofuranyl]carbonyl]amino]-
1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

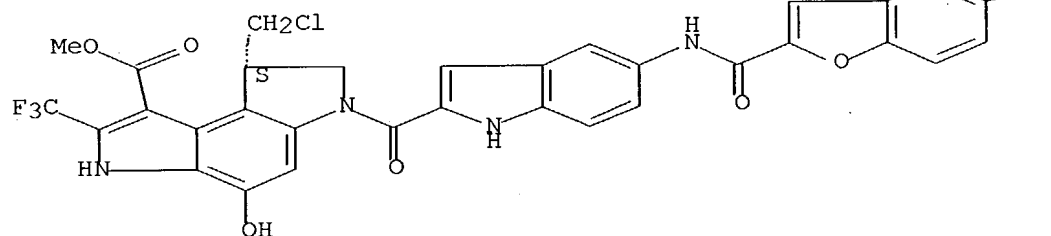


RN 157823-25-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[[[5-methoxy-2-benzofuranyl]carbonyl]amino]-
1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



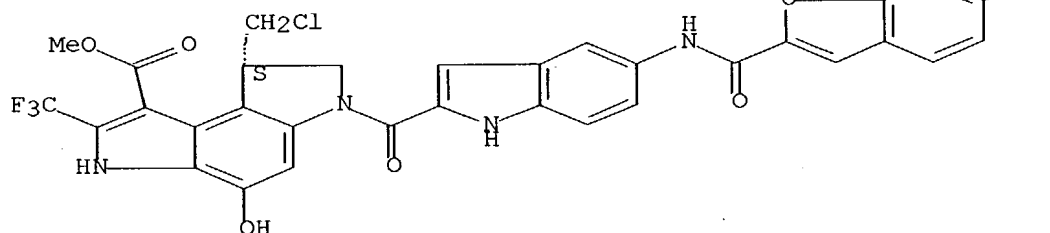
PAGE 1-B

—OMe

RN 157823-26-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[6-methoxy-2-benzofuranyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

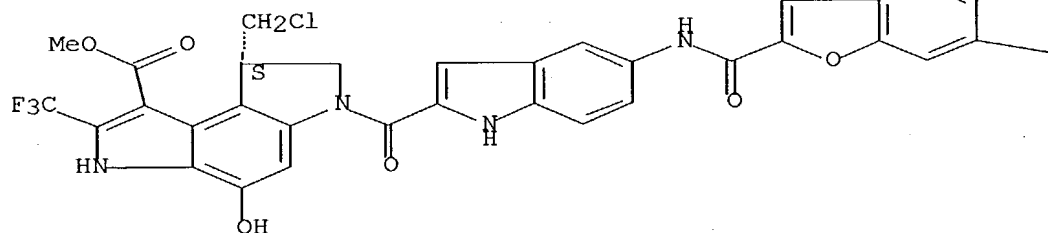
—OMe

RN 157823-27-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-
[[[6-(diethylamino)-2-benzofuranyl]carbonyl]amino]-1H-indol-2-
yl]carbonyl]-
3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



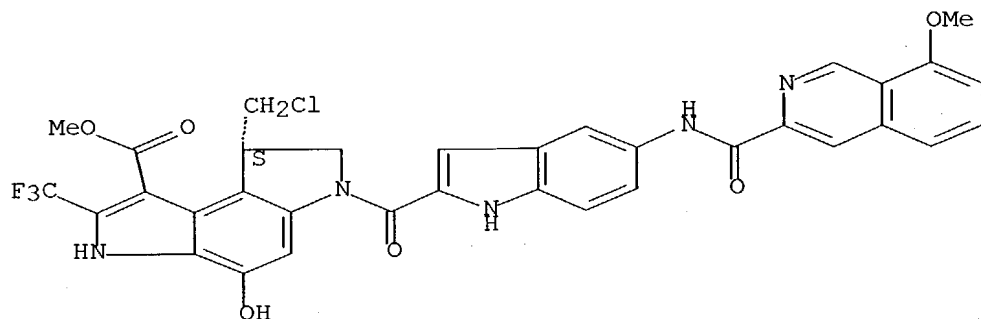
PAGE 1-B

—NEt₂

RN 157823-28-4 CAPLUS

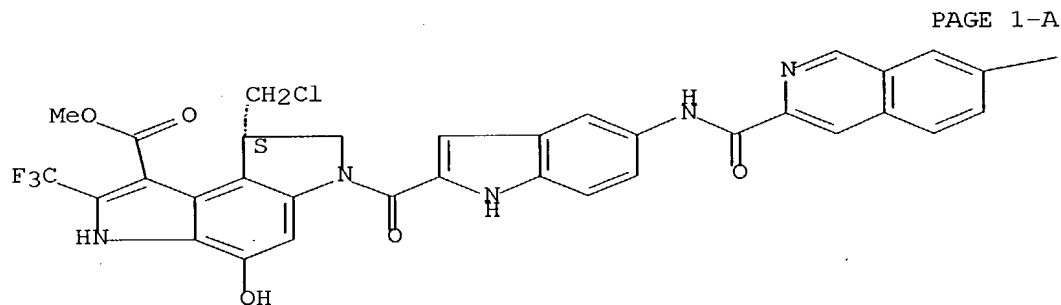
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[[[8-methoxy-3-isoquinolinyl]carbonyl]amino]-
1H-
indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 157823-29-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[(7-methoxy-3-isoquinolinyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).



PAGE 1-A

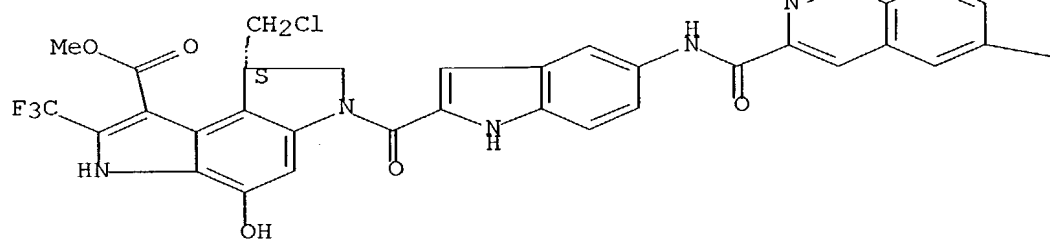
—OMe

PAGE 1-B

RN 157823-30-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[[(6-methoxy-3-isoquinolinyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A

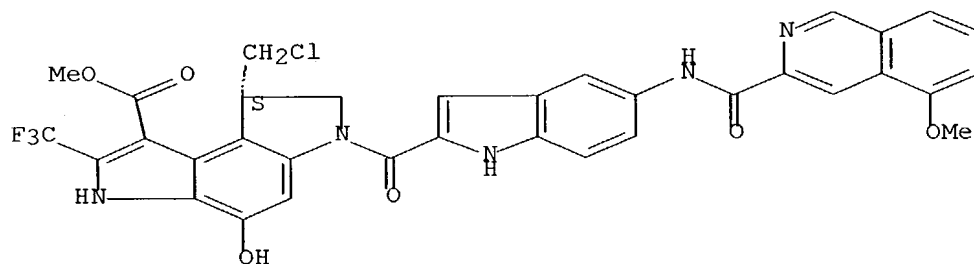


PAGE 1-B

—OMe

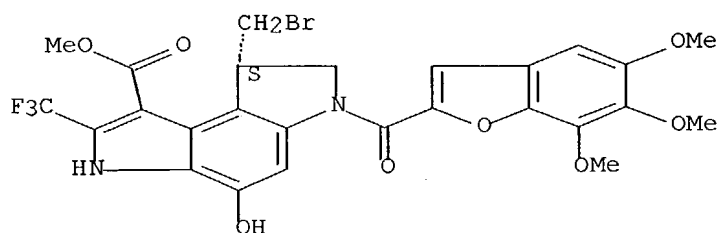
RN 157823-31-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[(5-methoxy-3-isoquinolinyl)carbonyl]amino]-
 1H-
 indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 157823-39-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-2-
 benzofuranyl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

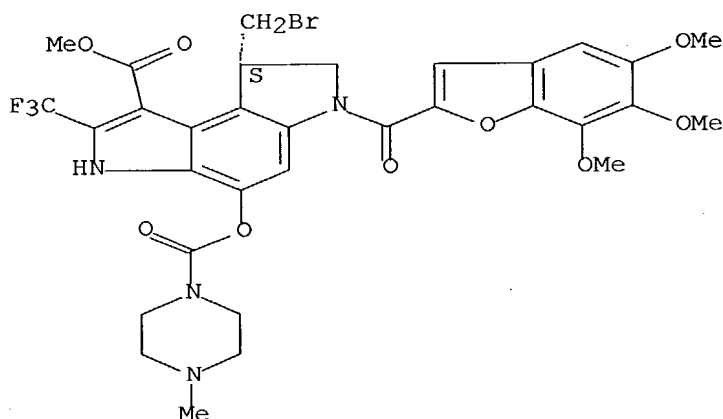


RN 157823-40-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-2-(trifluoromethyl)-6-[[(5,6,7-trimethoxy-2-benzofuranyl) carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

● HCl

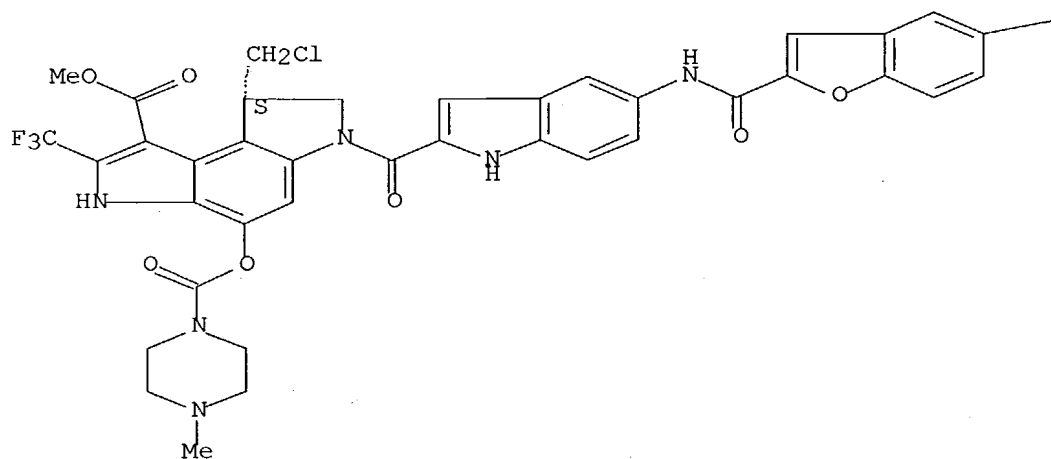
RN 157823-41-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(5-methoxy-2-benzofuranyl) carbonyl] amino]-1H-indol-2-yl] carbonyl]-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-2-(trifluoromethyl)-

, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

—OMe

● HCl

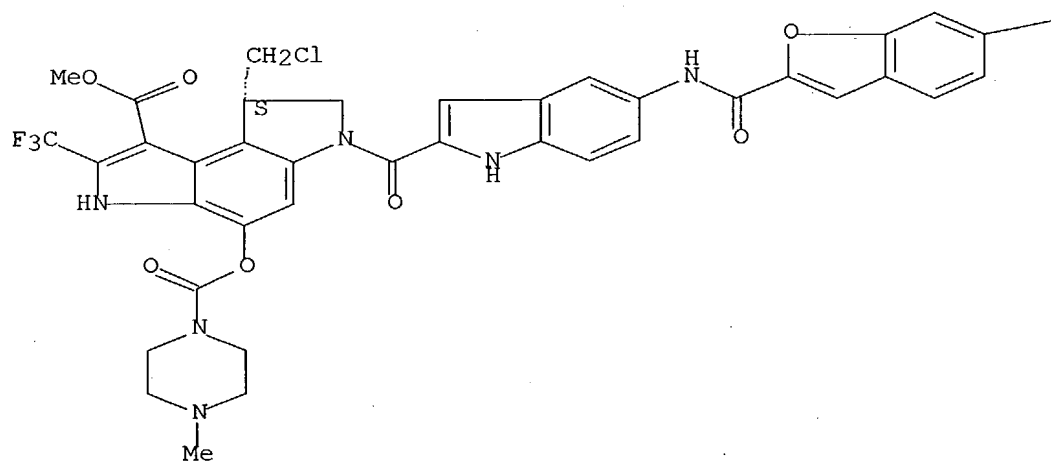
RN 157823-42-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-6-[[5-[[[(6-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-
yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-
(trifluoromethyl)-

, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

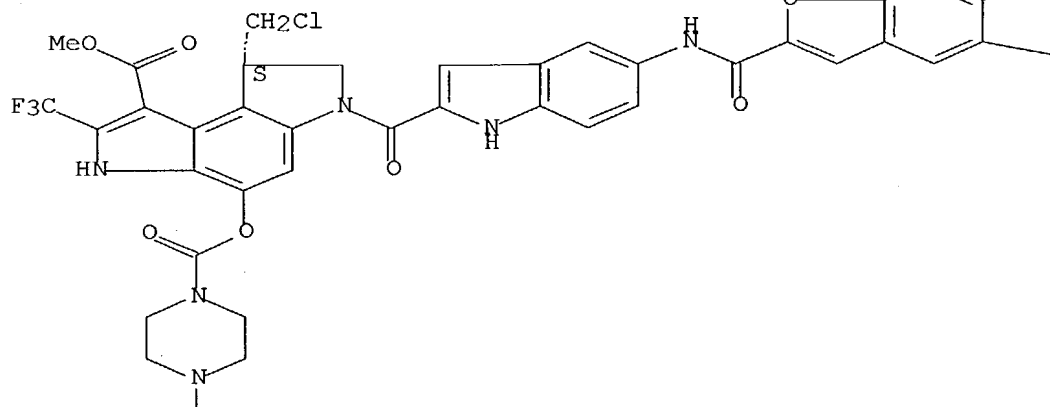


—OMe

● HCl

RN 157823-43-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-6-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-2-
 (trifluoromethyl)-
 6-[[5-[[(5,6,7-trimethoxy-2-benzofuranyl) carbonyl]amino]-1H-indol-2-
 yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX
 NAME)

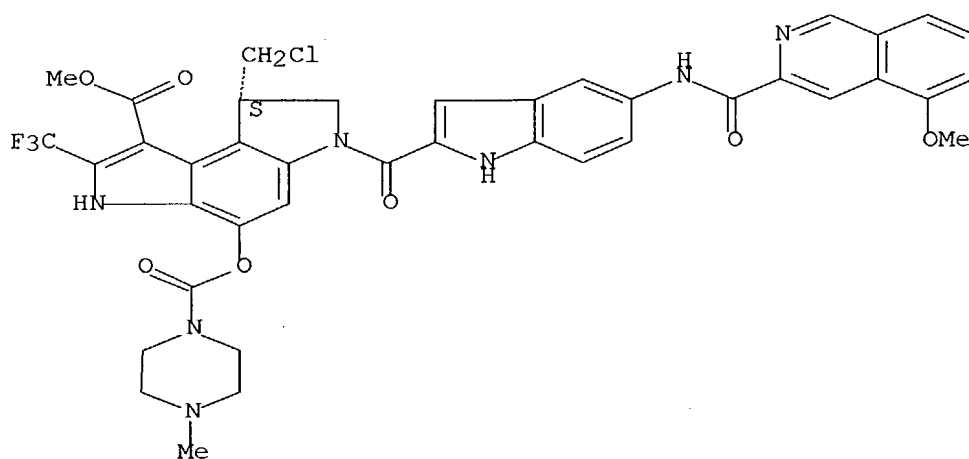
Absolute stereochemistry. Rotation (+).

 ---OMe — OMe
$$\text{Me}$$

● HCl

RN 157823-44-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-6-[[5-[[(5-methoxy-3-isoquinolinyl) carbonyl] amino]-1H-indol-
2-
yl] carbonyl]-4-[[(4-methyl-1-piperazinyl) carbonyl] oxy]-2-
(trifluoromethyl)-
, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

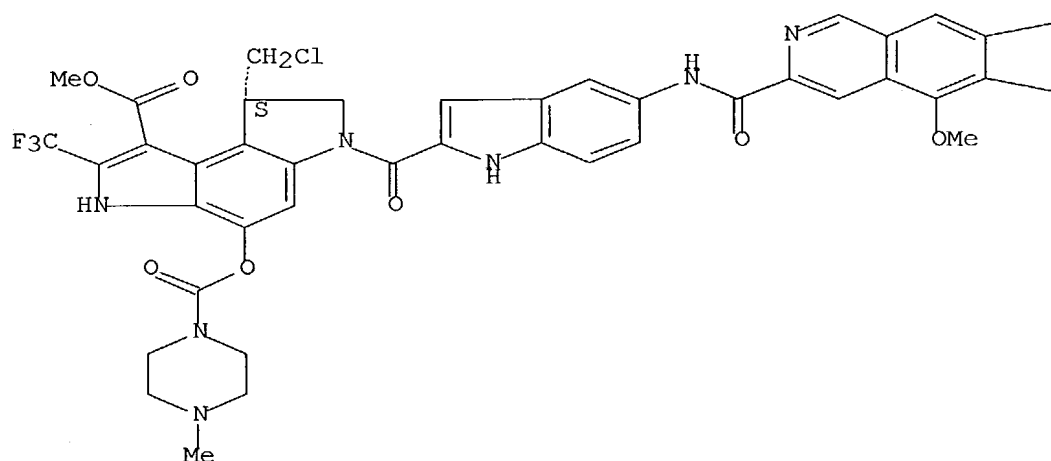


● HCl

RN 157823-45-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-2-
(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-3-isoquinolinyl]carbonyl]amino]-1H-indol-2-
yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry. Rotation (+).



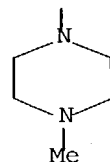
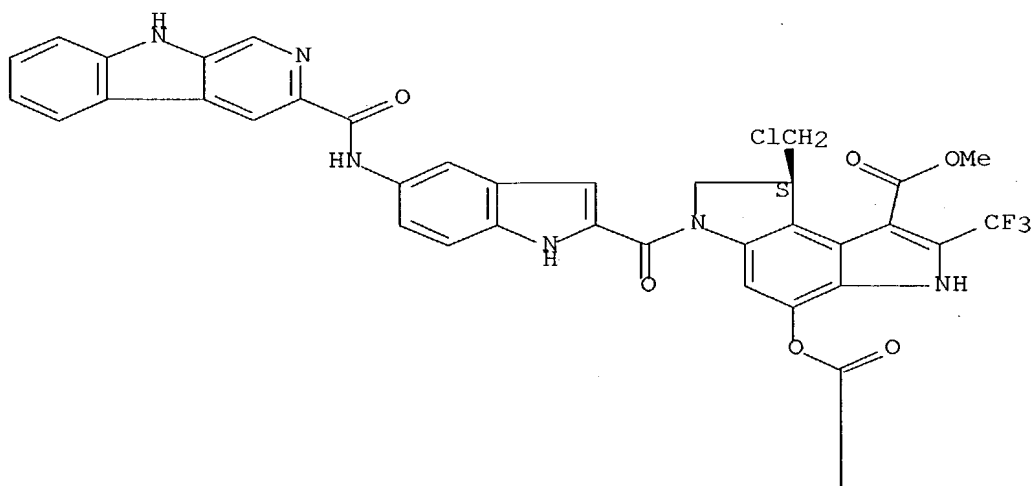
—OMe

—OMe

● HCl

RN 157823-46-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[5-[(9H-
 pyrido[3,4-
 b]indol-3-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-
 methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

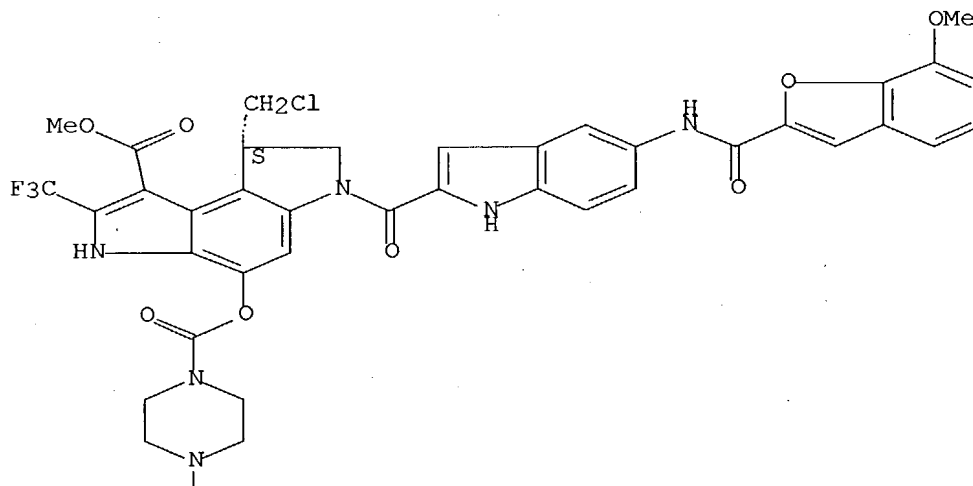
Absolute stereochemistry.



● HCl

RN 157823-47-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-
 yl]carbonyl]-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-
 (trifluoromethyl)-
 , methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



Me

RN 157823-48-8 CAPLUS

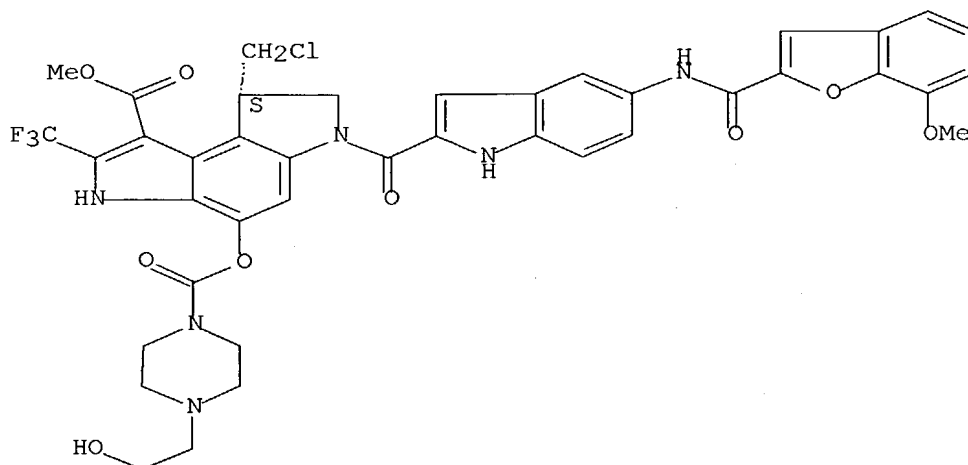
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[[4-(2-hydroxyethyl)-1-piperazinyl]carbonyl]oxy]-6-[[5-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA

INDEX

NAME)

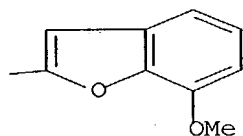
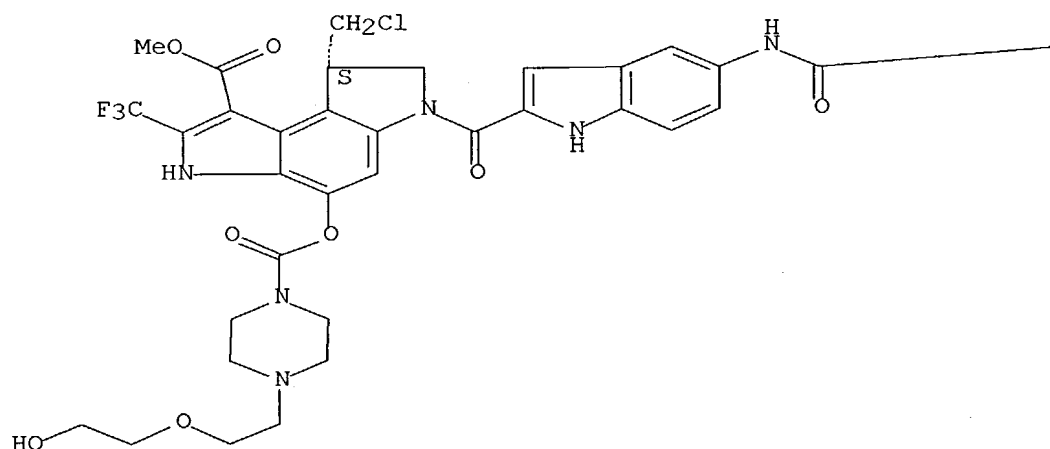
Absolute stereochemistry.



● HCl

RN 157823-49-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[[4-[2-(2-hydroxyethoxy)ethyl]-1-
 piperazinyl]carbonyl]oxy]-6-
 [[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-
 2-
 (trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA
 INDEX
 NAME)

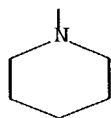
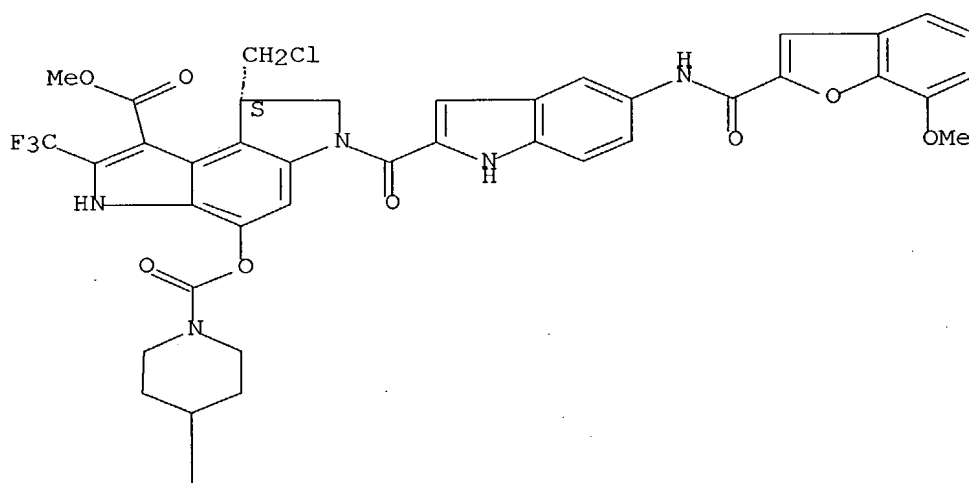
Absolute stereochemistry.



● HCl

RN 157823-50-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-
 1'-ylcarbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(7-methoxy-
 2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
 (trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

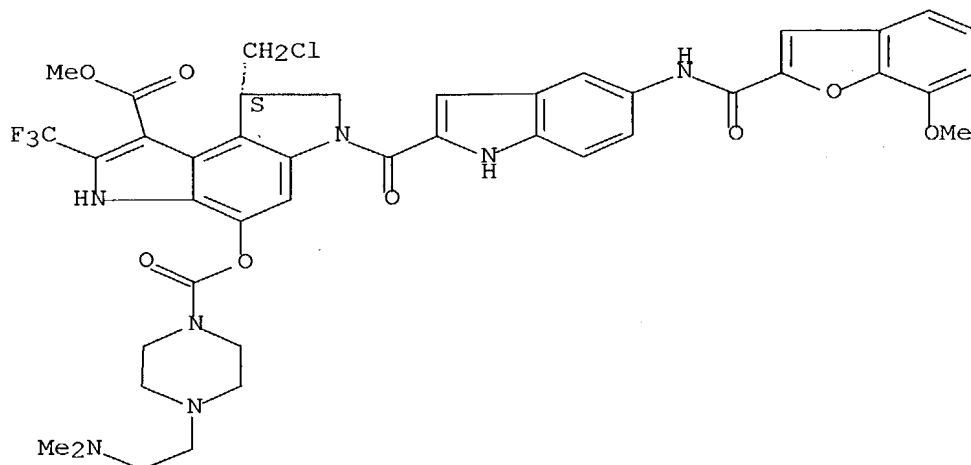
Absolute stereochemistry.



● HCl

RN 157823-51-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[4-(dimethylamino)ethyl]-1-piperazinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

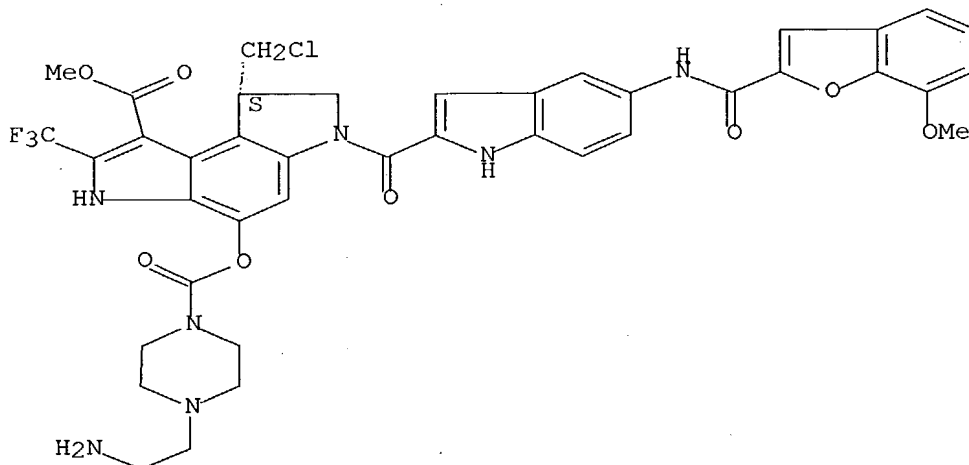


● 2 HCl

RN 157823-52-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[4-(2-aminoethyl)-1-piperazinyl]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-methoxy-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

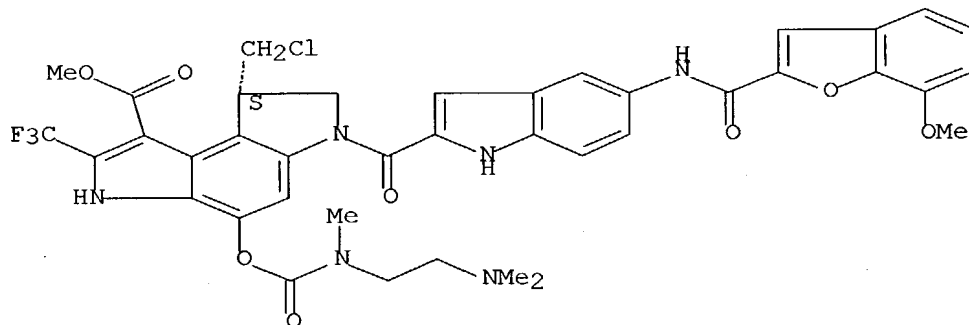
Absolute stereochemistry.



● 2 HCl

RN 157823-53-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-
 [[[[2-(dimethylamino)ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-
 [[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(
 (trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA
 INDEX
 NAME)

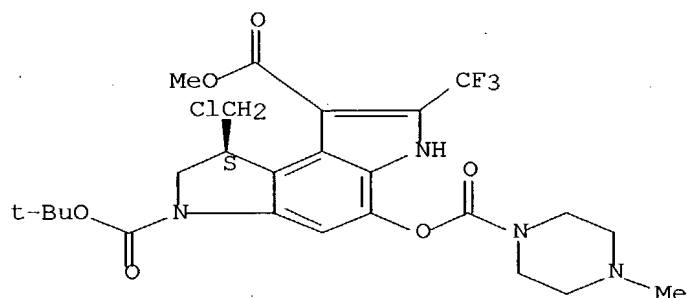
Absolute stereochemistry.



● HCl

RN 157823-54-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-
 2-
 (trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI)
 (CA INDEX NAME)

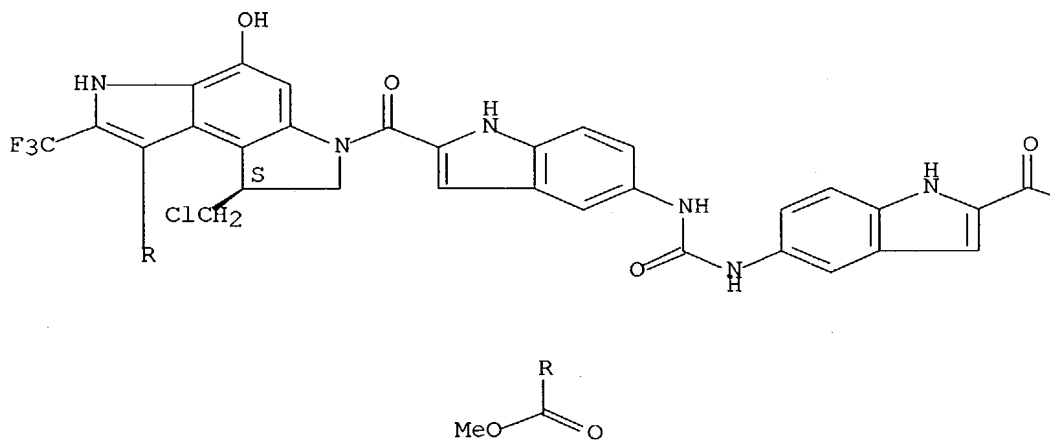
Absolute stereochemistry.

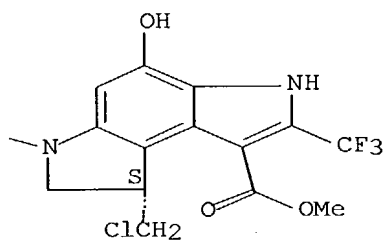


RN 157823-55-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[carbonylbis(imino-
 1H-
 indole-5,2-diylcarbonyl)]bis[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-4-
 hydroxy-2-(trifluoromethyl)-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

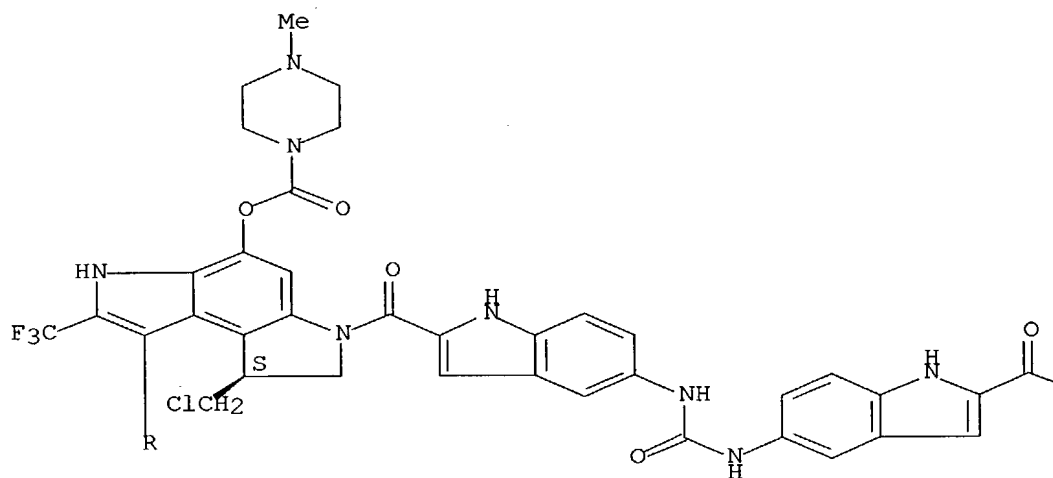
PAGE 1-A



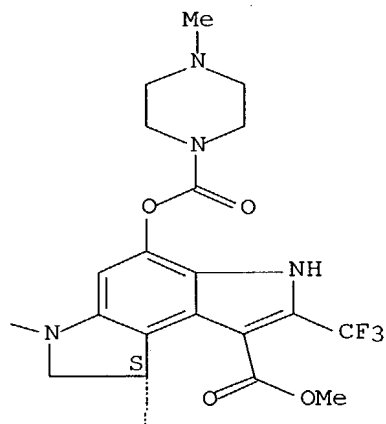


RN 157823-56-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[carbonylbis(imino-
 1H-indole-5,2-diylcarbonyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[4-
 methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, dimethyl ester,
 [S-(R*,R*)]-(9CI) (CA INDEX NAME)

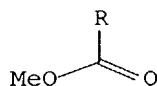
Absolute stereochemistry.



PAGE 1-B



PAGE 2-A

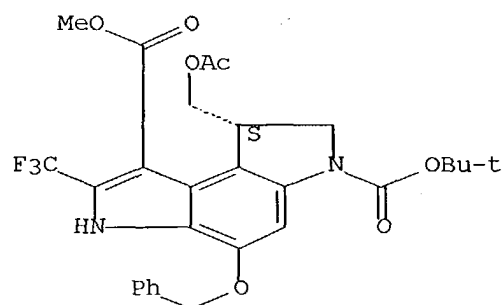


PAGE 2-B



RN 157904-26-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

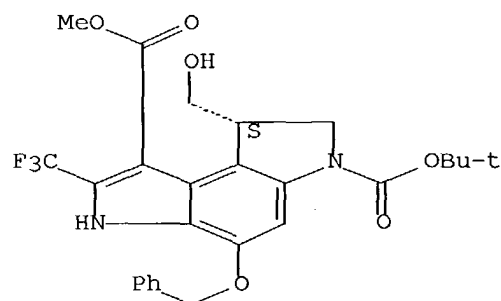
Absolute stereochemistry. Rotation (-).



RN 157904-27-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

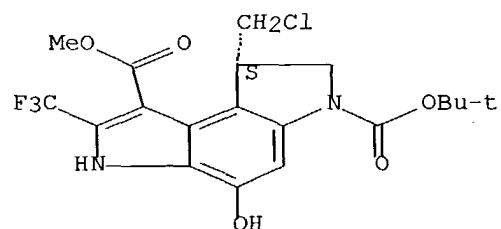
Absolute stereochemistry. Rotation (-).



RN 157904-28-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

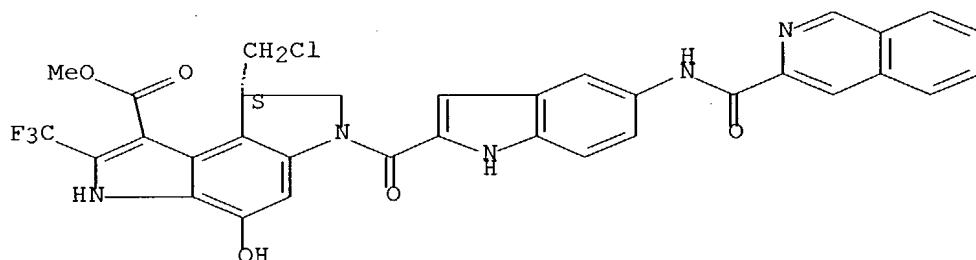
Absolute stereochemistry.



RN 157904-29-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-
yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

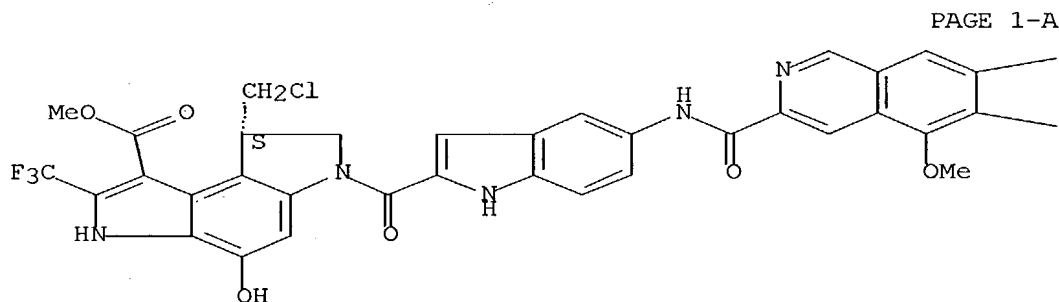
Absolute stereochemistry. Rotation (+).



RN 157904-30-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-3-
isoquinolinyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

—OMe

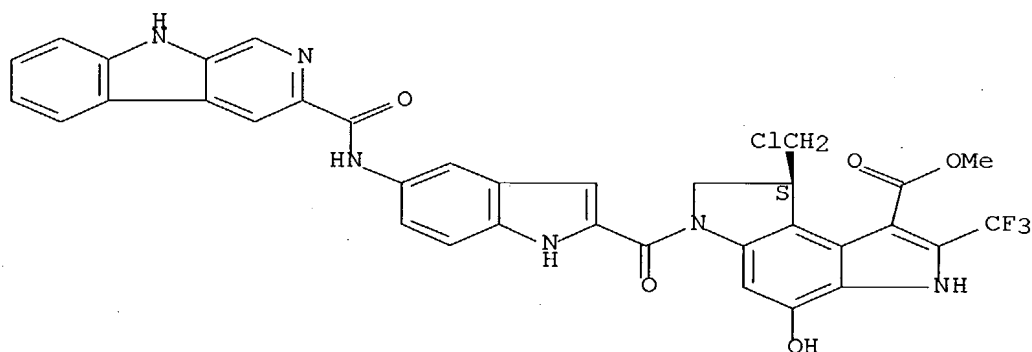
—OMe

PAGE 1-B

RN 157904-31-9 CAPLUS

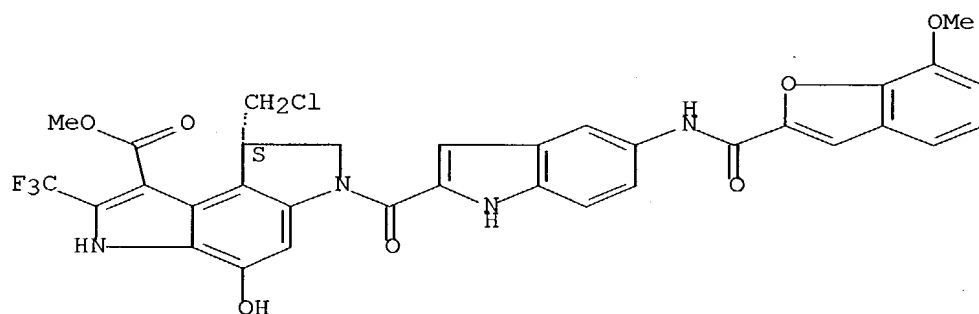
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[(9H-pyrido[3,4-b]indol-3-ylcarbonyl)amino]-
 1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



RN 157904-32-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[[5-[[7-methoxy-2-benzofuranyl]carbonyl]amino]-
 1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

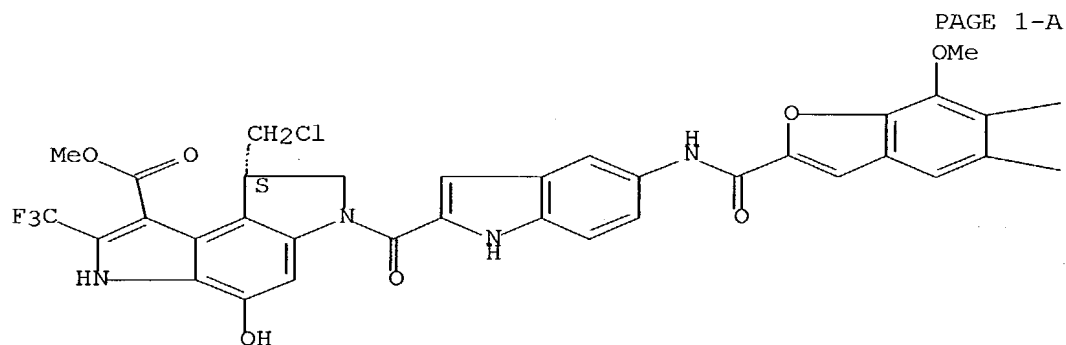


RN 157904-33-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-(trifluoromethyl)-6-[[5-[[5,6,7-trimethoxy-2-
 benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester,

(8S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



PAGE 1-B

—OMe

—OMe

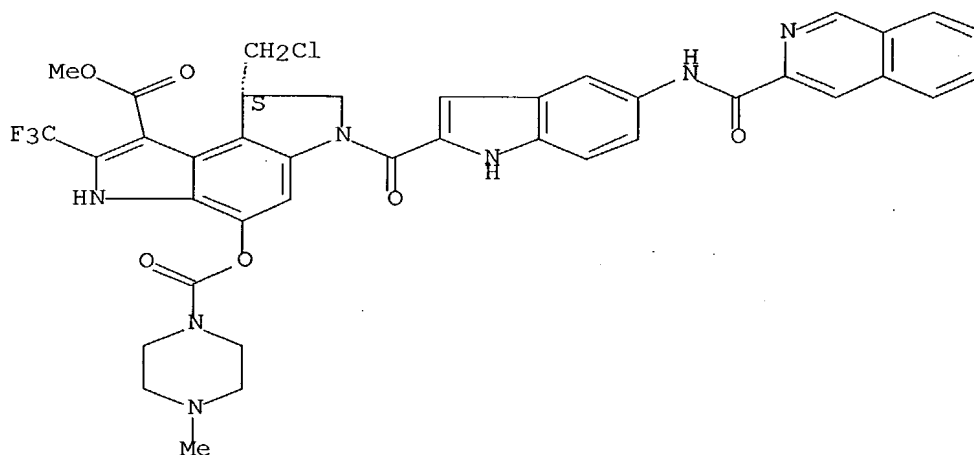
RN 157904-34-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-

tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-
yl]carbonyl]-

4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl
ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

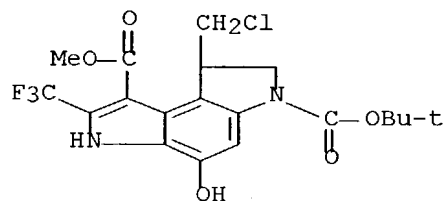
Absolute stereochemistry. Rotation (+).



● HCl

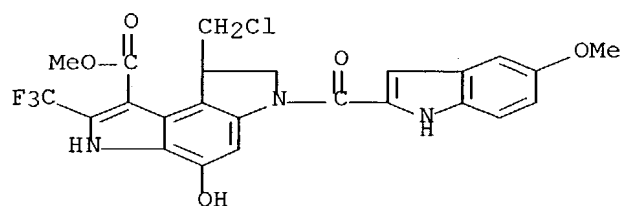
RN 194093-65-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-(trifluoromethyl)-,
 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-68-0 CAPLUS

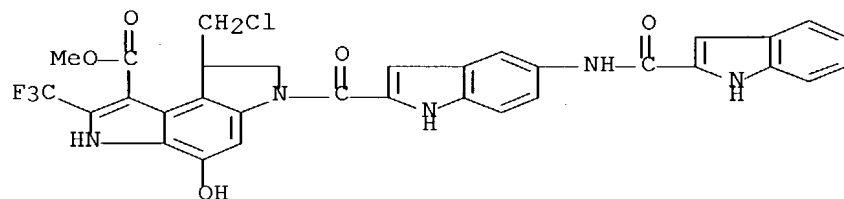
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-2-
 (trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 194093-70-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)

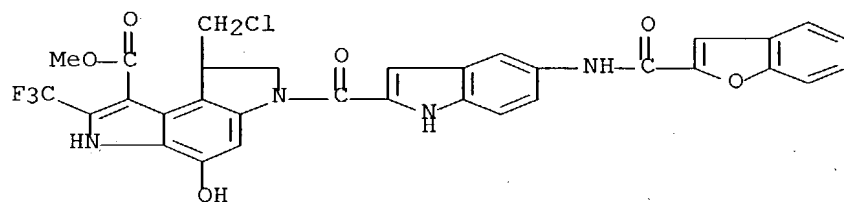


RN 194093-71-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI)

(CA

INDEX NAME)



L10 ANSWER 81 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

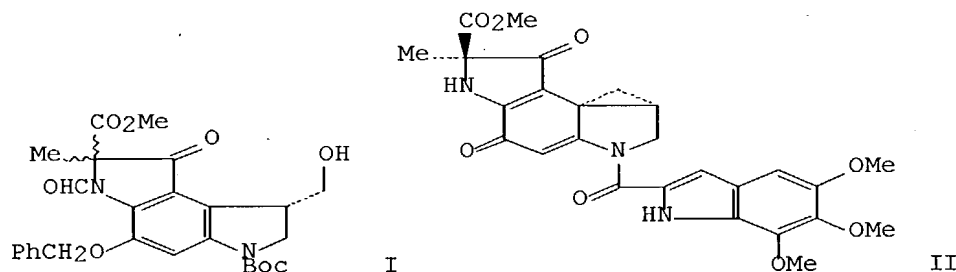
AN 1994:557348 CAPLUS Full-text

DN 121:157348

TI Synthetic studies on duocarmycin. 2. Synthesis and cytotoxicity of natural

(+)-duocarmycin A and its three possible stereoisomers

AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Terashima, Shiro
 CS Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Tochigi, 329-01, Japan
 SO Tetrahedron (1994), 50(9), 2809-20
 CODEN: TETRAB; ISSN: 0040-4020
 DT Journal
 LA English
 GI



AB The title synthesis was achieved by featuring the optical resolution of two types of the tricyclic intermediates, e.g., I, and the synthetic scheme established in the synthesis of racemic compds. In vitro cytotoxicity assay against P388 murine leukemia obviously showed that the absolute configuration of cyclopropane moiety in (+)-duocarmycin A (II) is closely related to its cytotoxicity.

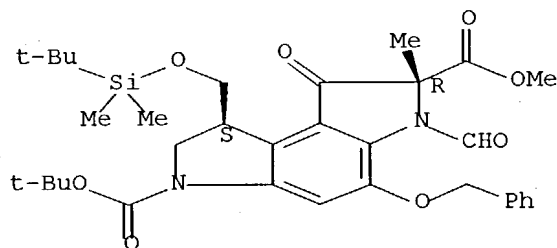
IT 132628-67-2 132628-68-3

RL: RCT (Reactant); RACT (Reactant or reagent)
 (desilylation of)

RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
 tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

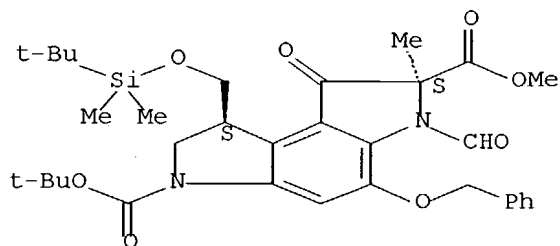


RN 132628-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
 tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)

2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 149365-66-2P 149365-67-3P

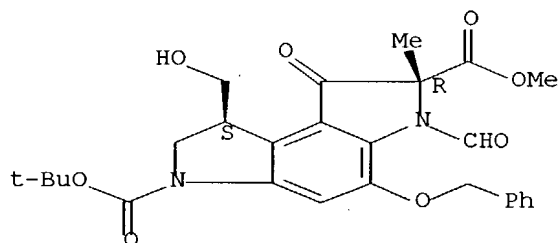
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with acetylmandelic acid)

RN 149365-66-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI)

(CA
INDEX NAME)

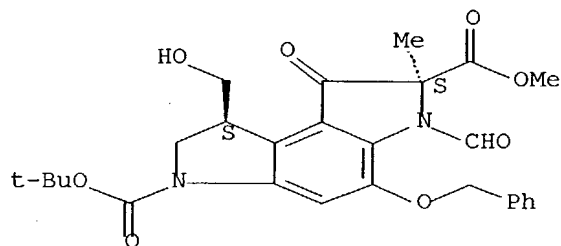
Relative stereochemistry.



RN 149365-67-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid,
6-formyl-1,6,7,8-tetrahydro-1-(hydroxymethyl)-7-methyl-8-oxo-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) 7-methyl ester, cis- (9CI) (CA
INDEX NAME)

Relative stereochemistry.



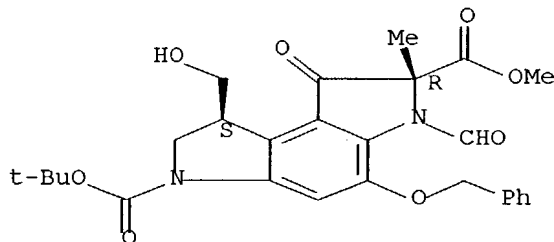
IT 157478-14-3P 157478-15-4P 157478-16-5P
157478-17-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to
(indolylcarbonyl)benzodipyrrolecarboxylat
e)

RN 157478-14-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)-
(9CI)
(CA INDEX NAME)

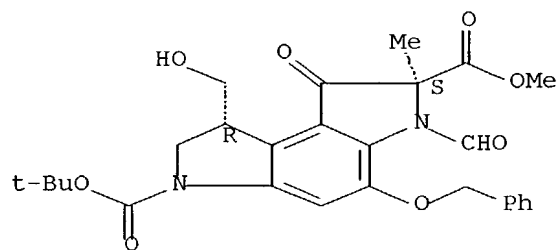
Absolute stereochemistry.



RN 157478-15-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2S-trans)-
(9CI)
(CA INDEX NAME)

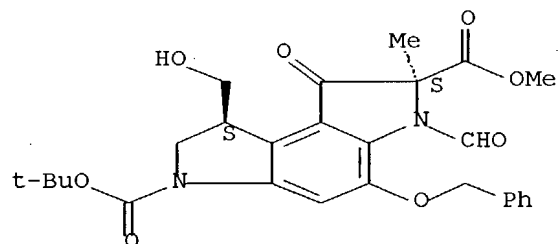
Absolute stereochemistry.



RN 157478-16-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2S-cis)- (9CI)
(CA INDEX NAME)

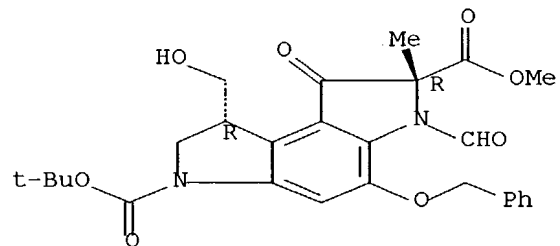
Absolute stereochemistry.



RN 157478-17-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-cis)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT 157478-24-5P 157478-25-6P 157478-26-7P
157478-27-8P

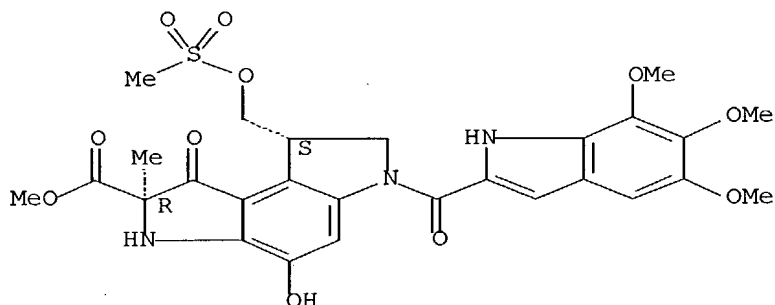
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and conversion of, to duocarmycin A isomer)

RN 157478-24-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



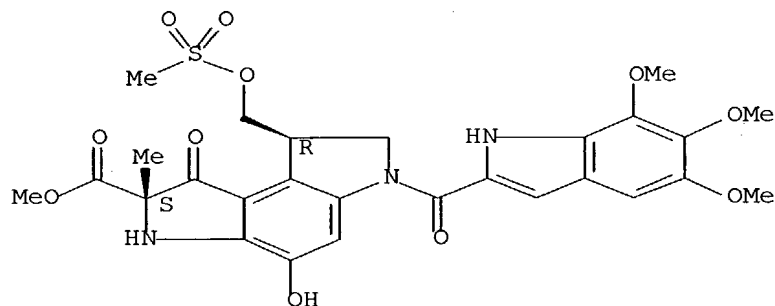
RN 157478-25-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI)

(CA

INDEX NAME)

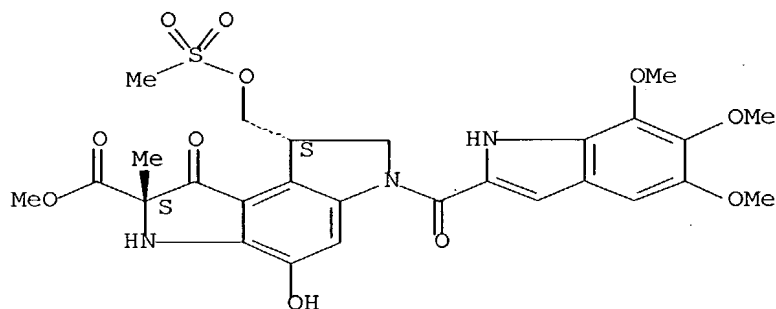
Absolute stereochemistry. Rotation (-).



RN 157478-26-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

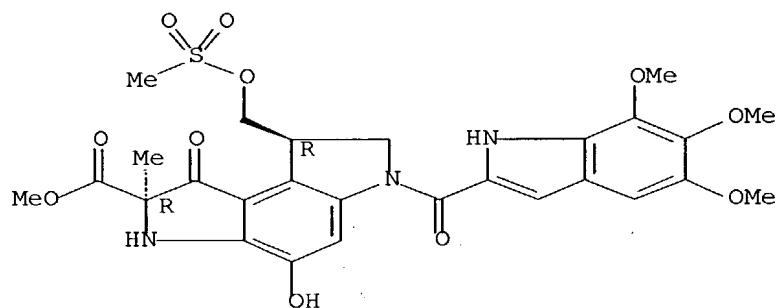
Absolute stereochemistry. Rotation (-).



RN 157478-27-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 157478-20-1P 157478-21-2P 157478-22-3P

157478-23-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and debenzylation of)

RN 157478-20-1 CAPLUS

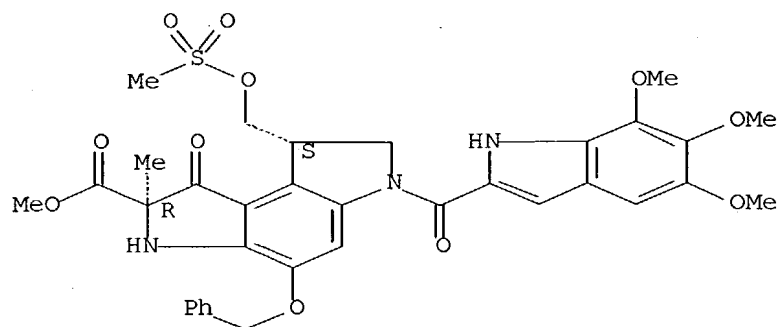
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-

trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI)

(CA

INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 157478-21-2 CAPLUS

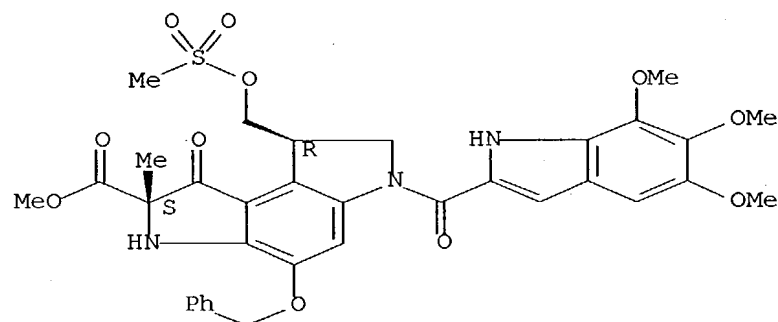
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI)

(CA

INDEX NAME)

Absolute stereochemistry. Rotation (-).

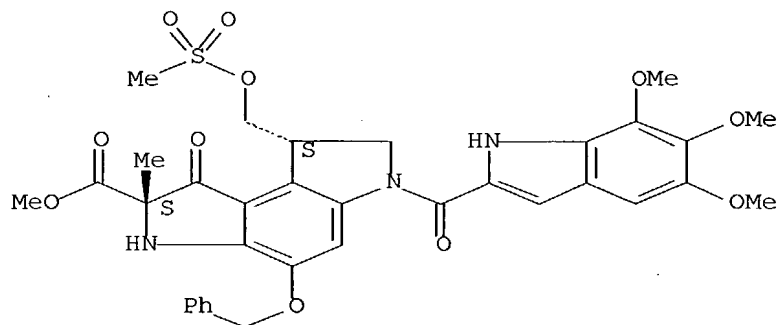


RN 157478-22-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

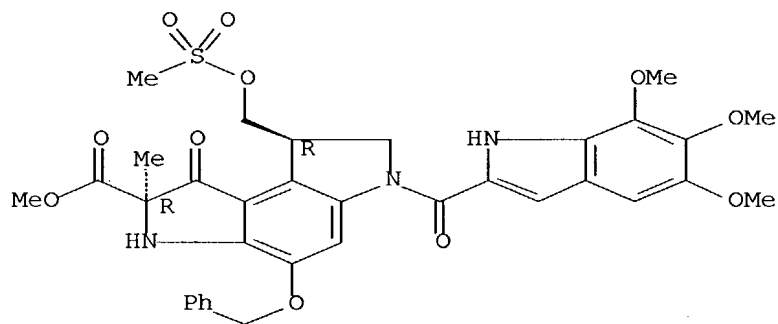
Absolute stereochemistry. Rotation (-).



RN 157478-23-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 157478-33-6P 157478-34-7P

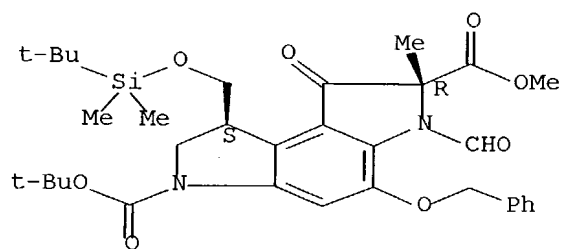
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)
(preparation and desilylation of)

RN 157478-33-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

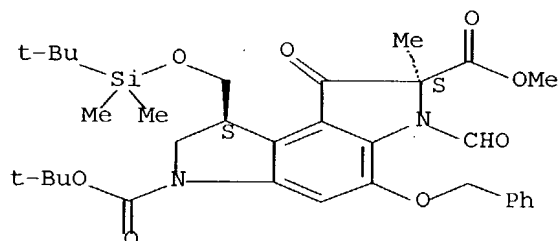
Absolute stereochemistry. Rotation (+).



RN 157478-34-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 149365-68-4P 149405-52-7P 149405-56-1P
149405-57-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

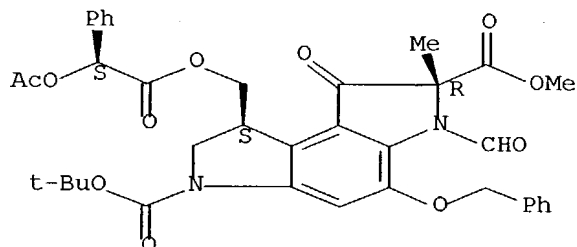
RACT

(Reactant or reagent)
(preparation and hydrolysis of)

RN 149365-68-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-
methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester,
[2R-[2 α ,8 β (S*)]]- (9CI) (CA INDEX NAME)

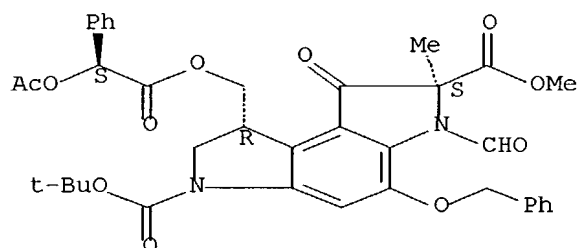
Absolute stereochemistry. Rotation (+).



RN 149405-52-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-
methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2S-[2 α ,8 β (R*)]]- (9CI) (CA INDEX NAME)

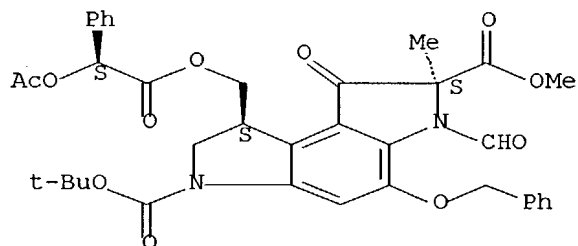
Absolute stereochemistry. Rotation (-).



RN 149405-56-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-
methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2S-[2 α ,8 α (R*)]]- (9CI) (CA INDEX NAME)

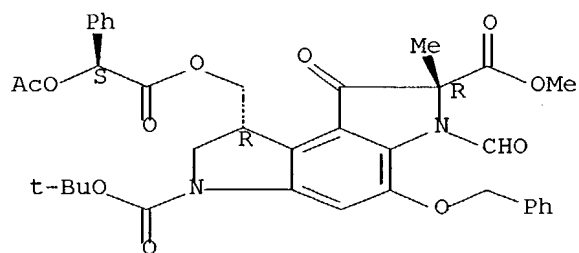
Absolute stereochemistry. Rotation (-).



RN 149405-57-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-
methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2R-[2 α ,8 α (S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 149405-53-8P 149405-54-9P 157478-18-7P
157478-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and mesylation of)

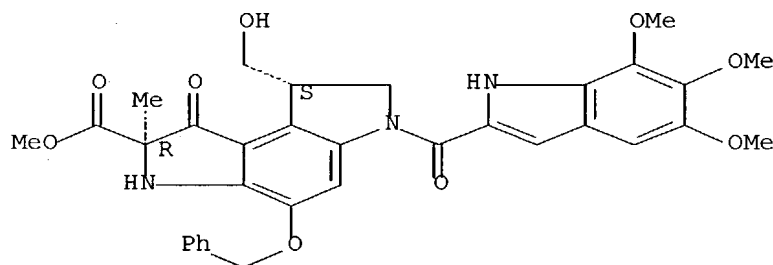
RN 149405-53-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-

1H-

indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



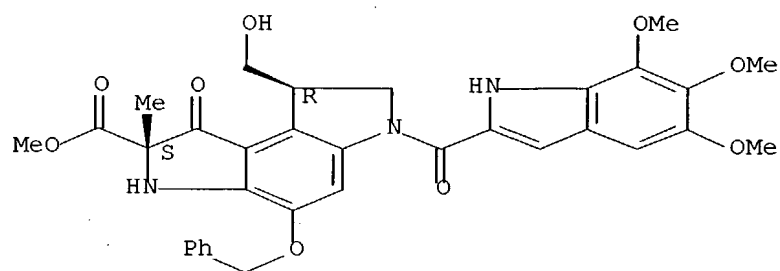
RN 149405-54-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-

1H-

indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

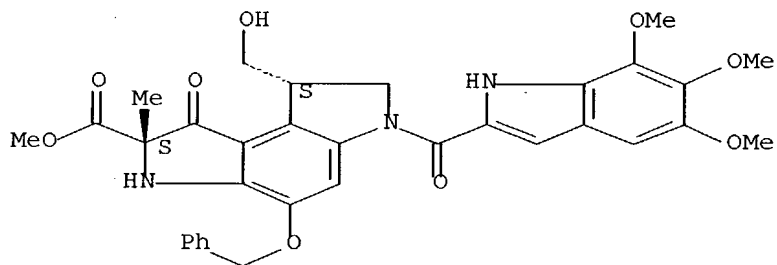
Absolute stereochemistry. Rotation (-).



RN 157478-18-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

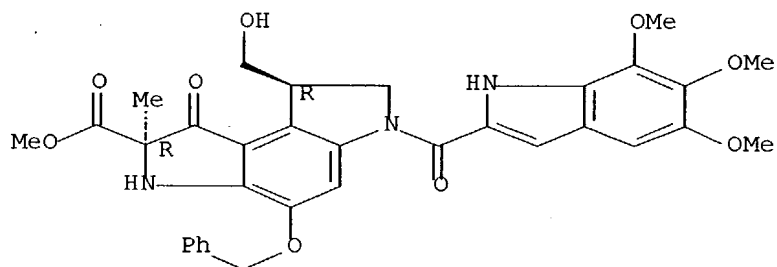
Absolute stereochemistry. Rotation (-).



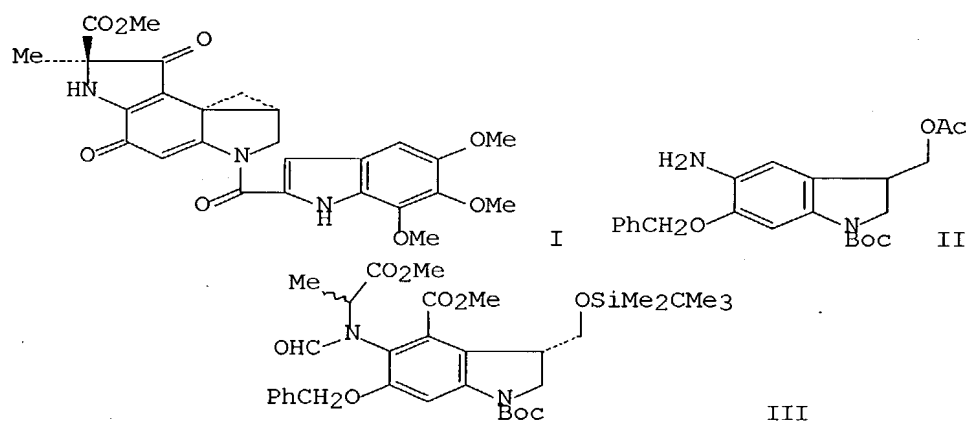
RN 157478-19-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L10 ANSWER 82 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:557347 CAPLUS Full-text
 DN 121:157347
 TI Synthetic studies on duocarmycin. 1. Total synthesis of dL-duocarmycin A and its 2-epimer
 AU Fukuda, Yasumichi; Itoh, Yoshio; Nakatani, Kazuhiko; Terashima, Shiro
 CS Sagami Chem. Res. Cent., Kanagawa, 229, Japan
 SO Tetrahedron (1994), 50(9), 2793-808
 CODEN: TETRAB; ISSN: 0040-4020
 DT Journal
 LA English
 OS CASREACT 121:157347
 GI



AB The title synthesis of dL-duocarmycin A (I) and its 2-epimer was first achieved by employing novel methoxycarbonylation of the C4-position of the 5-aminoindoline II by way of the isatin and subsequent Dieckmann cyclization of indolecarboxylate III to the Me 2-methylindoxyl-2-carboxylate as key steps. In vitro cytotoxicity assay against P388 murine leukemia obviously disclosed that cytotoxicities of the synthesized compds. are comparable and almost half of that of natural (+)-duocarmycin A.

IT 132628-69-4P 143314-85-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

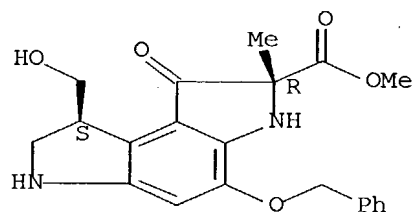
(Reactant or reagent)

(preparation and acylation of, with indolecarboxylic acid)

RN 132628-69-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, methyl ester, dihydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

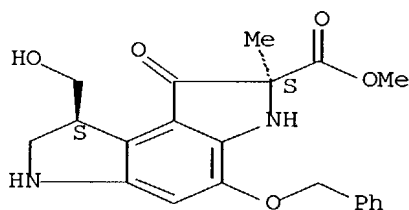


●2 HCl

RN 143314-85-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, methyl ester, dihydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



●2 HCl

IT 157485-14-8P 157485-15-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and cyclization of)

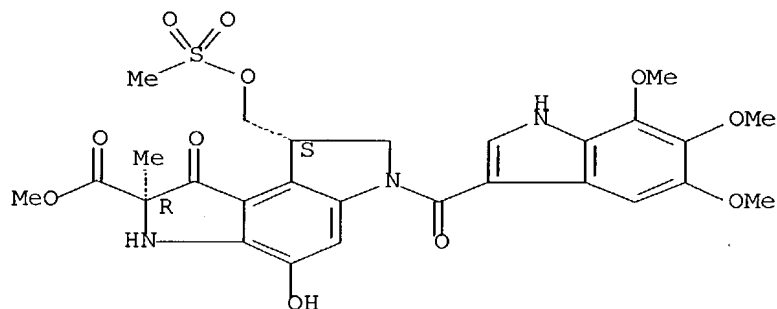
RN 157485-14-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, trans- (9CI) (CA

INDEX

NAME)

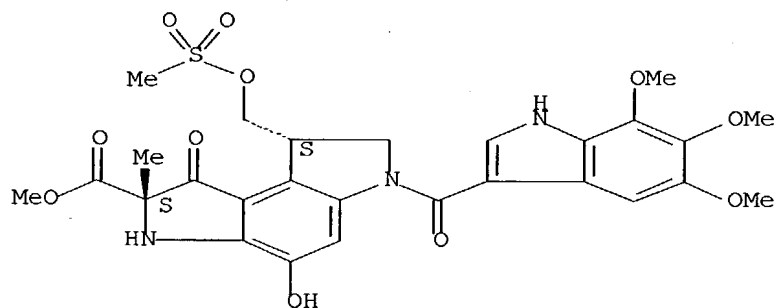
Relative stereochemistry.



RN 157485-15-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 157485-12-6P 157485-13-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

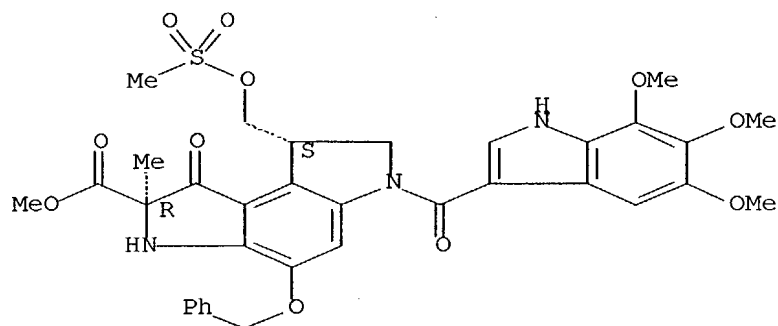
(Reactant or reagent)

(preparation and hydrogenation of)

RN 157485-12-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

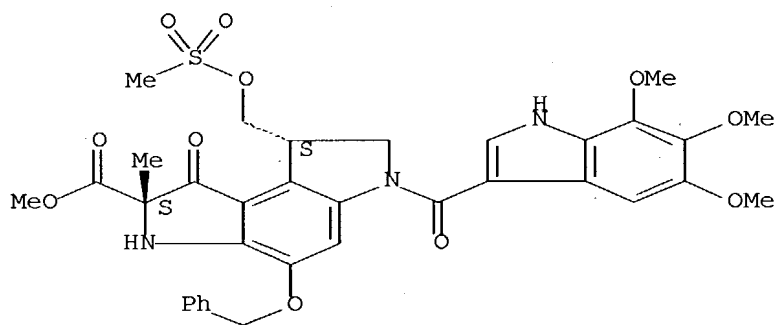
Relative stereochemistry.



RN 157485-13-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 132628-67-2P 132628-68-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

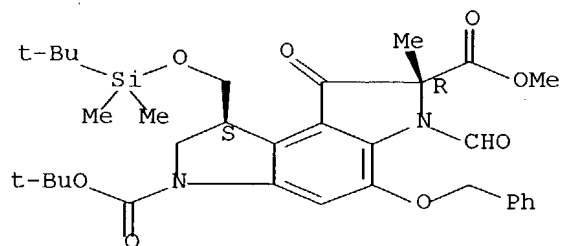
RACT

(Reactant or reagent)
(preparation and hydrolysis of)

RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

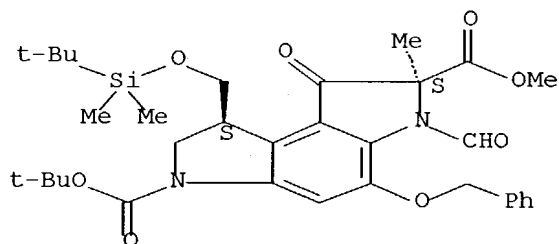
Relative stereochemistry.



RN 132628-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 157485-10-4P 157485-11-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and mesylation of)

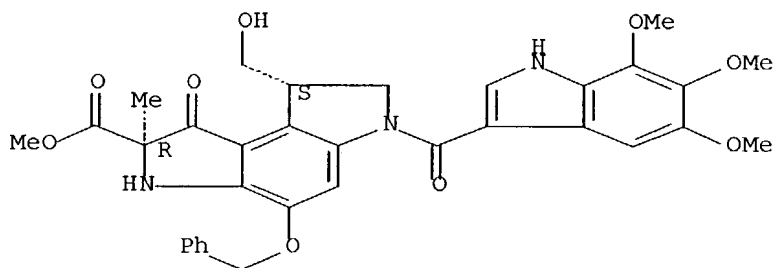
RN 157485-10-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-

1H-

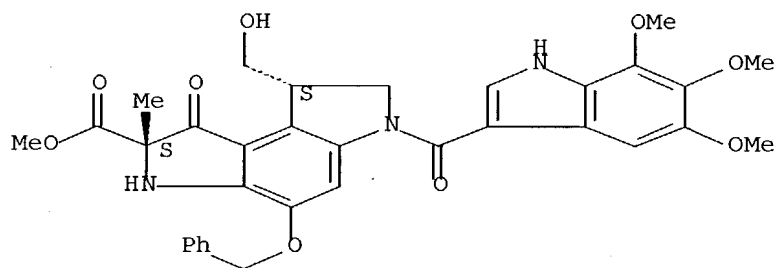
indol-3-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 157485-11-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L10 ANSWER 83 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:548428 CAPLUS Full-text
DN 121:148428
TI A novel antitumor antibiotic, KW-2189, is activated by carboxyl esterase and induces DNA strand breaks in human small cell lung cancer cells
AU Ogasawara, Hayato; Nishio, Kazuto; Takeda, Yuichiro; Ohmori, Tohru; Kubota, Naohiro; Funayama, Yasunori; Ohira, Tatsuo; Kuraishi, Yasunobu; Isogai, Yukihide; Saijo, Nagahiro
CS Pharmacol. Div., Natl. Cancer Center Res. Inst., Tokyo, 104, Japan
SO Japanese Journal of Cancer Research (1994), 85(4), 418-25
CODEN: JJCREP; ISSN: 0910-5050
DT Journal
LA English
AB The purpose of this study was to examine the DNA-binding potency and the mechanisms of cytotoxicity of KW-2189. In order to analyze the DNA-binding activity of KW-2189, plasmid pBR322 was treated with KW-2189 with or without pretreatment with carboxyl esterase, and the products were examined by agarose gel electrophoresis and restriction enzyme anal. Cytotoxic activity was examined by exposing a human small-cell lung cancer cell line, NCI-H69, to KW-2189 with or without carboxyl esterase. Alkaline elution was performed to examine whether KW-2189 induces DNA strand breaks. DNA treated with KW-2189 and carboxyl esterase migrated faster than DNA treated with KW-2189 alone, which migrated at the same rate as untreated DNA. In addition DNA treated with esterase-activated KW-2189 was protected from digestion by some restriction enzymes. KW-2189 had concentration- and time-dependent growth inhibitory effects, with IC50 values from 58 mM (96 h) to 1900 nM (1 h) in H69 cells. The IC50 values for 4-h exposure of H69 to KW-2189 plus 0, 26, 130, and 650 mU carboxyl esterase/mL were 460, 120, 30, and 7 nM, resp. Time-dependent enhancement of cytotoxicity by carboxyl esterase was also observed KW-2189 induced DNA strand breaks in H69

cells in a concentration-dependent manner around the IC50 value.
Apparently: (1) KW-2189 is activated by carboxyl esterase to its active form(s); (2) activated KW-2189 has a stronger DNA-binding activity and cytotoxicity than KW-2189 alone; (3) DNA cleavage is one of the major mechanisms of KW-2189-mediated cytotoxicity.

IT 154889-68-6, KW 2189

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES

(Uses)

(neoplasm inhibition by, DNA damage as mechanism of, activation in relation to)

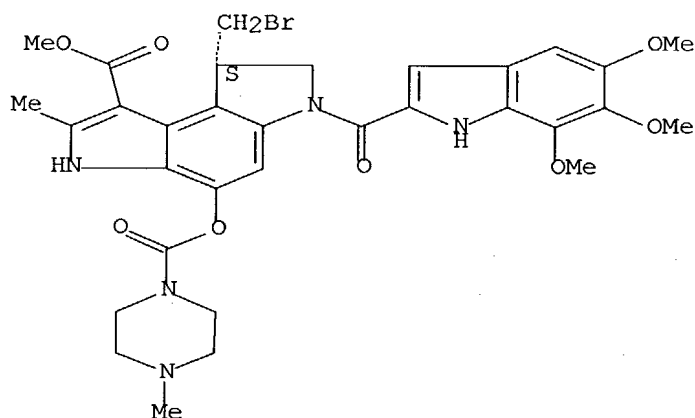
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



L10 ANSWER 84 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:508766 CAPLUS Full-text

DN 121:108766

TI Preparation of tetrahydropyrroloindoles as antitumor agents

IN Terajima, Atsuro; Fukuda, Yasumichi; Oomori, Yasuo

PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res

SO Jpn. Kokai Tokkyo Koho, 21 pp.

CODEN: JKXXAF

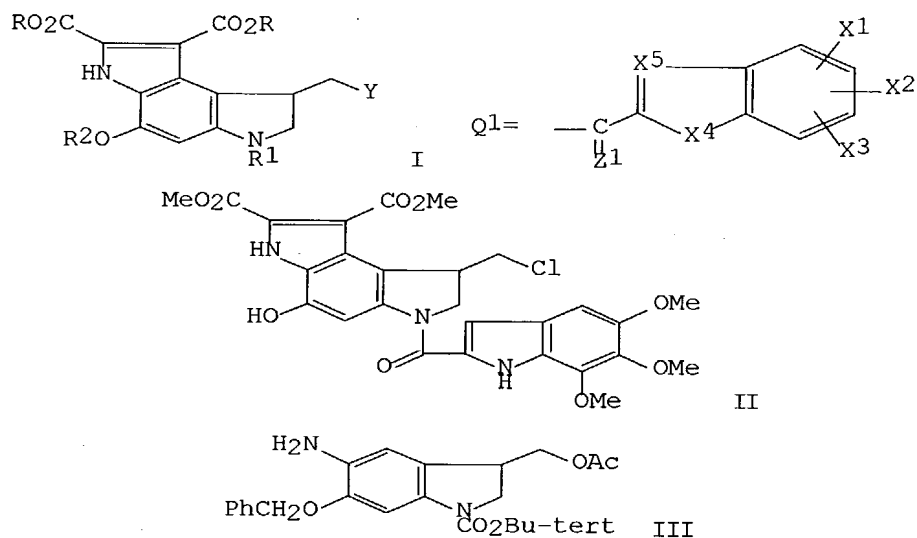
DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	JP 06122684	A2	19940506	JP 1992-274282	19921013
PRAI	JP 1992-274282		19921013		

OS MARPAT 121:108766
GI



AB The title compds., e. g., I [R = alkyl; R1 = Q1, etc.; X4 = O, S, NH; X5 = CH, N; X1 - X3 = H, OH, etc.; Z1 = O, S, etc.; R2 = H, OH-protecting group, etc.; Y = halo, etc.] are prepared. The title compound II was prepared in multiple steps from indoline derivative III. II in vitro showed IC50 of 0.31 ng/mL against P388 mouse leukemic cells.

IT **156905-81-6P 156905-82-7P 156905-83-8P**
156905-84-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

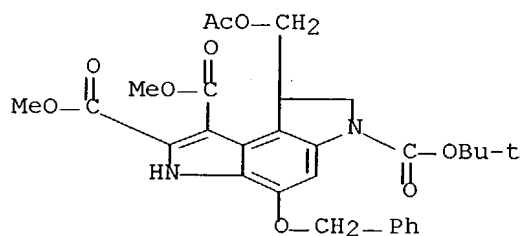
RACT

(Reactant or reagent)

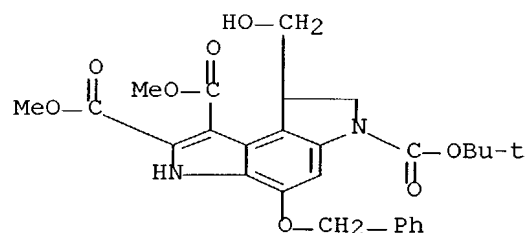
(preparation and reaction of, in preparation of antitumor agent)

RN 156905-81-6 CAPLUS

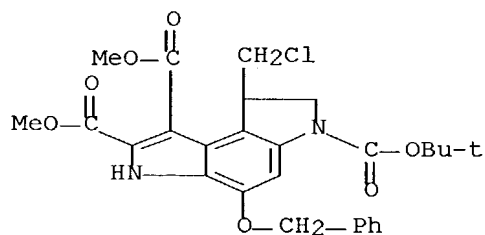
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid,
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-
dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



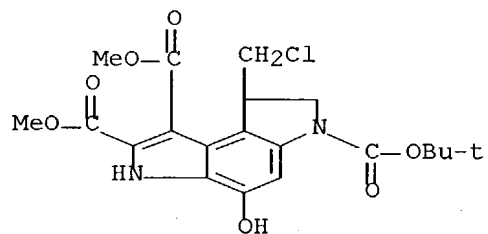
RN 156905-82-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid,
 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 1,2-dimethyl ester (9CI) (CA INDEX NAME)



RN 156905-83-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 1,2-dimethyl ester (9CI) (CA INDEX NAME)



RN 156905-84-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl)
 1,2-dimethyl ester (9CI) (CA INDEX NAME)



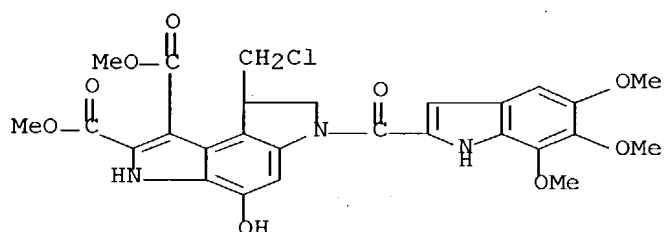
IT 156905-67-8P 156905-68-9P 156905-69-0P
156905-70-3P 156905-75-8P 156905-76-9P
156905-77-0P 156905-78-1P 156905-79-2P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antitumor agent)

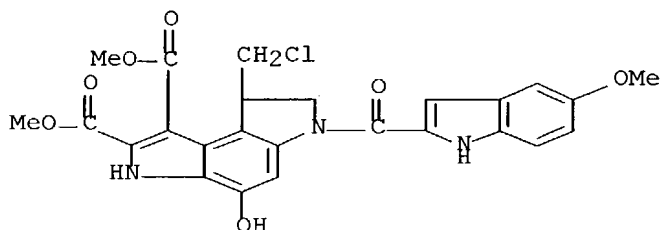
RN 156905-67-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-
yl)carbonyl]-
, dimethyl ester (9CI) (CA INDEX NAME)



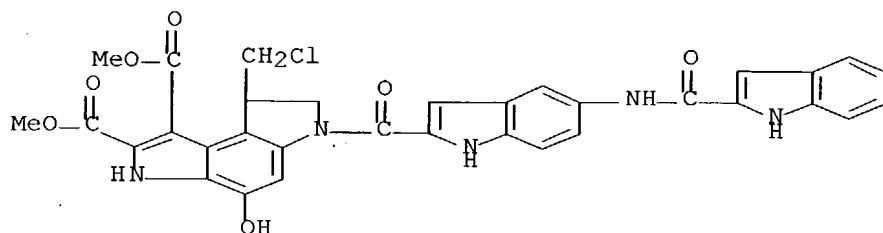
RN 156905-68-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-,
dimethyl ester (9CI) (CA INDEX NAME)



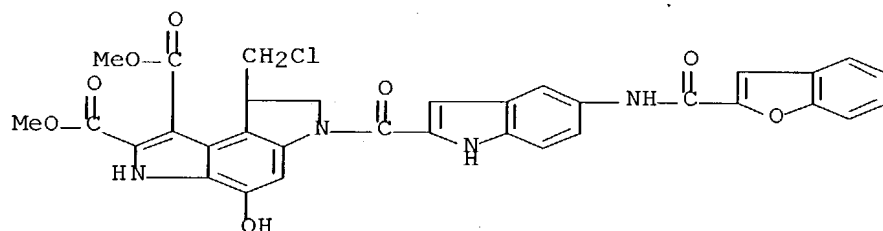
RN 156905-69-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-
indol-2-yl]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)



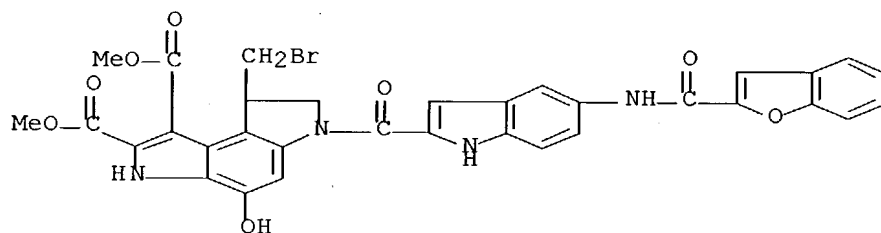
RN 156905-70-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-, dimethyl ester (9CI) (CA INDEX NAME)



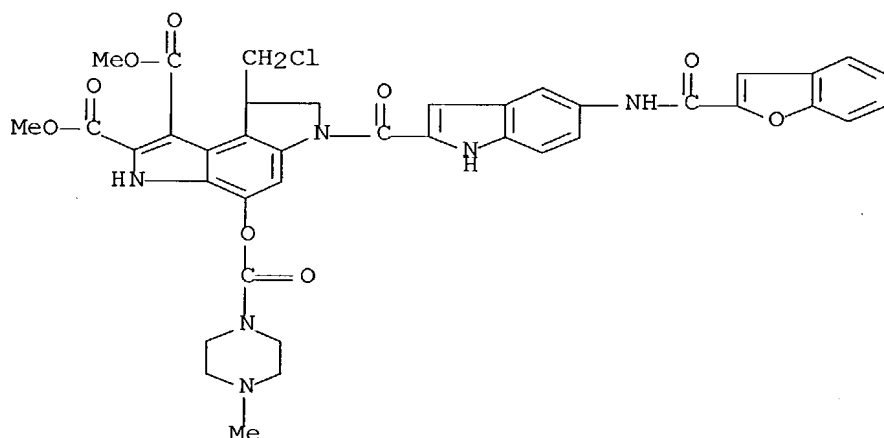
RN 156905-75-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-, dimethyl ester (9CI) (CA INDEX NAME)



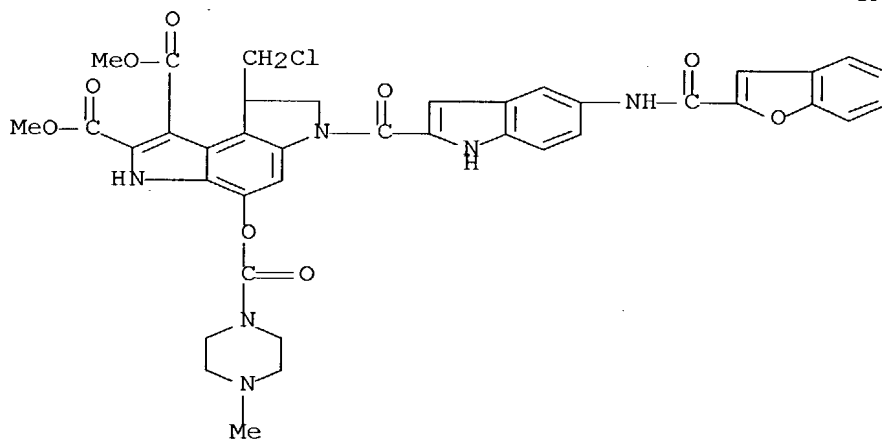
RN 156905-76-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 156905-77-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

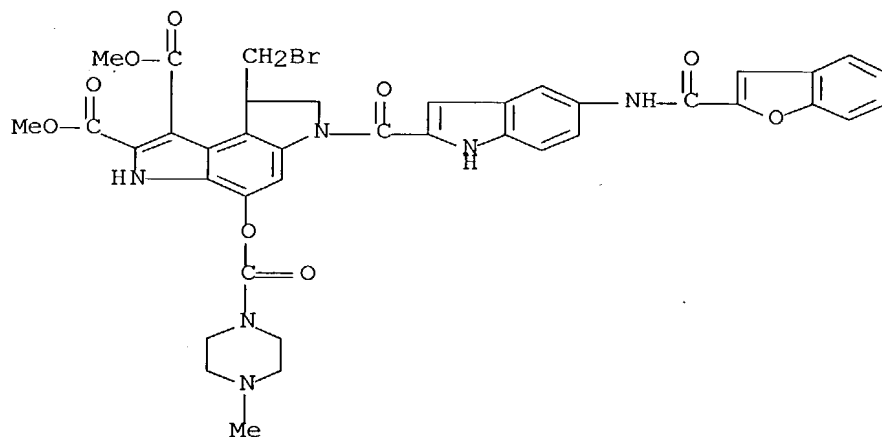


PAGE 2-A

● HCl

RN 156905-78-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, dimethyl

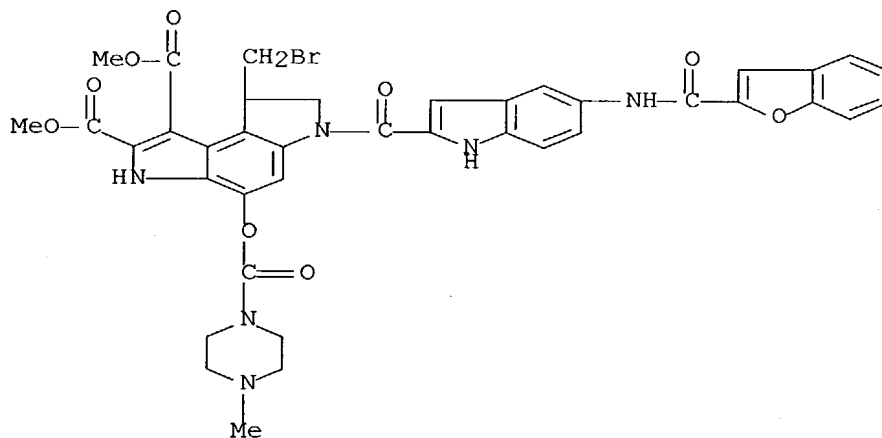
ester (9CI) (CA INDEX NAME)



RN 156905-79-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuran-5-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[4-methyl-1-piperazinyl]carbonyl]oxy]-, dimethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

● HCl

L10 ANSWER 85 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:483318 CAPLUS Full-text
 DN 121:83318
 TI Preparation of tetrahydropyrroloindole derivative and intermediates therefor
 IN Terashima, Shiro; Fukuda, Yasumichi
 PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center
 SO PCT Int. Appl., 24 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9404534	A1	19940303	WO 1993-JP1158	19930819
	W: AU, BB, BG, BR, CA, CZ, FI, HU, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	JP 06116270	A2	19940426	JP 1993-204254	19930818
	AU 9349811	A1	19940315	AU 1993-49811	19930819
PRAI	JP 1992-222861	A	19920821		
	JP 1993-204254	A	19930818		
	WO 1993-JP1158	W	19930819		
OS	CASREACT 121:83318; MARPAT 121:83318				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Tetrahydropyrroloindole derivs. (I; R1 = H or a hydroxyl-protecting group; R2 = H or an amino-protecting group; X = halo, OH, alkylcarbonyloxy, arylcarbonyloxy, alkylsulfonyloxy, arylsulfonyloxy) and optically active isomers thereof, useful as intermediates for a prospective anticancer agent KW-2189 (II.HCl), are prepared by reaction of aminoindoline derivs. (III; R = H; R3 = HO-protective group; R4 = H2N-protective group; X1 = protected HO) with MeC.tplbond.CCO2Me, MeCOCH2CO2Me, or substituted Me crotonate and cyclization of the resulting Me (indolinylamino)crotonate III (R = CMe:CHCO2Me; R3, R4, X1 = same as above) in the presence of a metal catalyst. Thus, (3S)-III (R = H, R3 = PhCH2, R4 = Me3CO2C, X1 = OAc), MeCOCH2CO2Me, and p-MeC6H4SO3H.H2O were refluxed in benzene at 80° for 4 h to give (3S)-III (R = CMe:CHCO2Me; R3, R4, X1 = same as above) which was heated in the presence of Pd(OAc)2 in DMF at 70° for 4 h to give (3S)-I (R3 = PhCH2, R4 = Me3CO2C, X1 = OAc). The latter compound was deacetylated with K2CO3 in MeOH and chlorinated by CCl4 and PPh3 in CH2Cl2 at room temperature to give (3S)-I (R3 = PhCH2, R4 = Me3CO2C, X1 = Cl) which was converted into (S)-KW-2189 II in 5 steps.

IT 156395-56-1, KW 2189

RL: RCT (Reactant); RACT (Reactant or reagent)
 (intermediates for, tetrahydropyrroloindole derivs. as)

RN 156395-56-1 CAPLUS

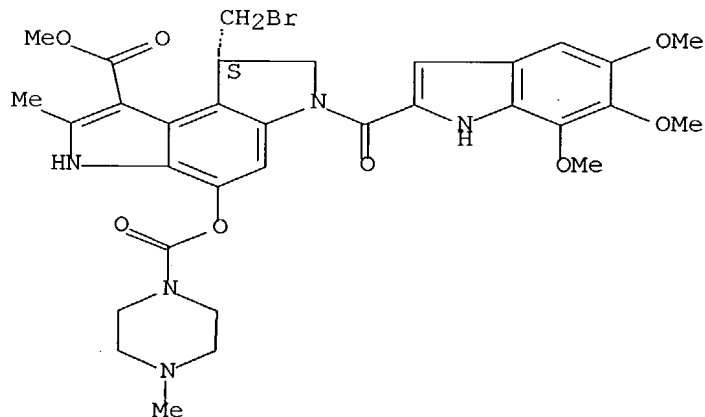
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride,

(S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

● HCl

IT 134106-67-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

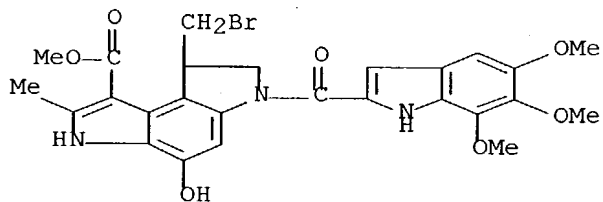
(Reactant or reagent)

(preparation and acylation of, by p-nitrophenyl chloroformate and N-methylpiperazine)

RN 134106-67-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-

, methyl ester (9CI) (CA INDEX NAME)



IT 156295-27-1P 156295-32-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

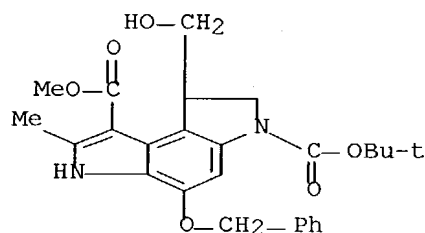
RACT

(Reactant or reagent)

(preparation and chlorination of, by carbon tetrachloride and triphenylphosphine)

RN 156295-27-1 CAPLUS

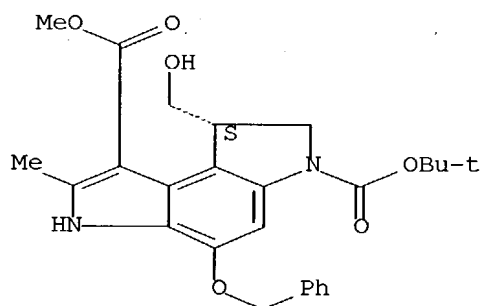
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 156295-32-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 156295-33-9P

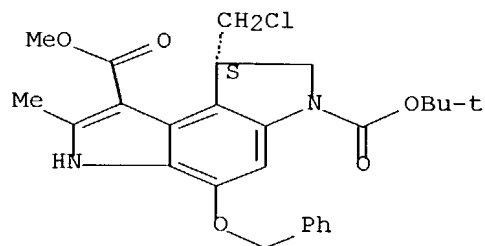
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation and conversion of, into anticancer KW-2189)

RN 156295-33-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 134106-66-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

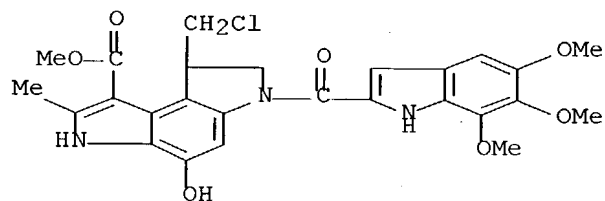
(preparation and cyclization of)

RN 134106-66-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-

, methyl ester (9CI) (CA INDEX NAME)



IT 156295-26-0P 156295-31-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

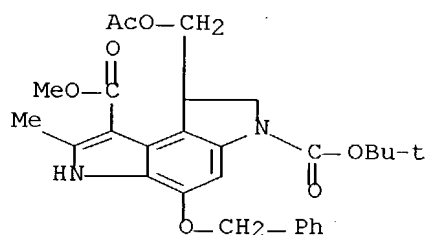
RACT

(Reactant or reagent)

(preparation and deacetylation of)

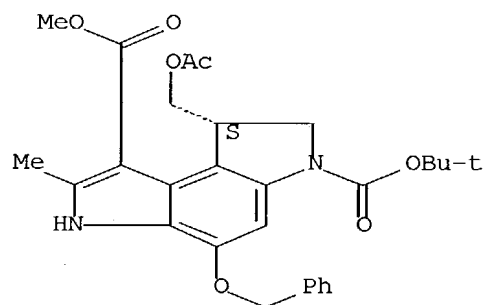
RN 156295-26-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

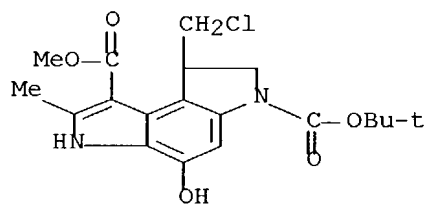


RN 156295-31-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,
 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 156295-28-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT
 (Reactant or reagent)
 (preparation and deprotection and acylation of, by
 trimethoxyindolecarboxylic acid)
 RN 156295-28-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
 8-(chloromethyl)-7,8-dihydro-4-hydroxy-2-methyl-, 6-(1,1-dimethylethyl)
 1-methyl ester (9CI) (CA INDEX NAME)



IT 156295-29-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

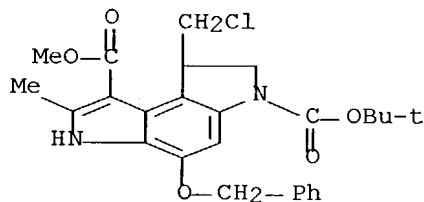
RACT

(Reactant or reagent)

(preparation and hydrogenolysis of)

RN 156295-29-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-,
6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



IT 134106-78-8P 134106-80-2P 154889-68-6P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

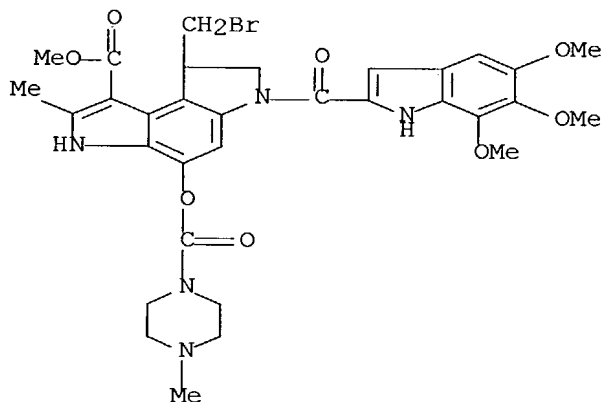
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of, as anticancer agent)

RN 134106-78-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

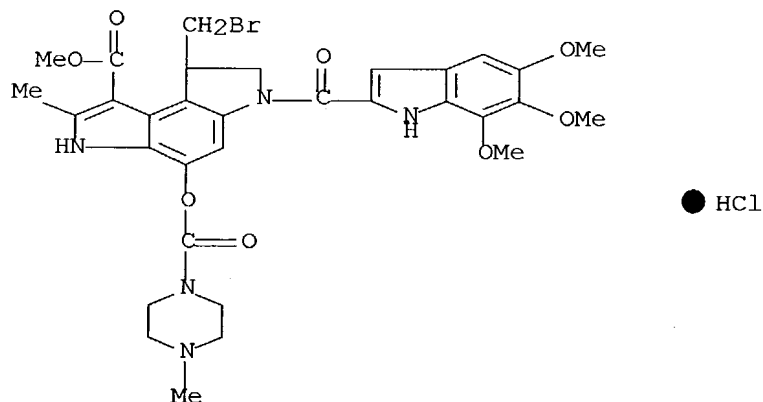


RN 134106-80-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride
(9CI)

(CA INDEX NAME)

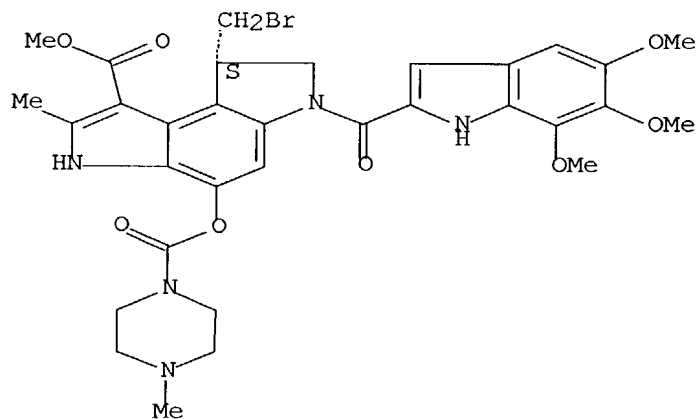


RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX
NAME)

Absolute stereochemistry.



L10 ANSWER 86 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:400322 CAPLUS Full-text

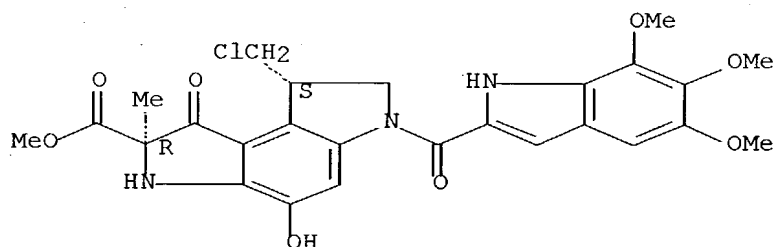
DN 121:322

TI Induction of endonucleolytic DNA fragmentation and apoptosis by the

duocarmycins

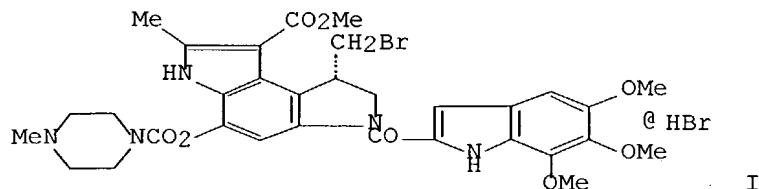
- AU Wrasidlo, W.; Johnson, Douglas S.; Boger, Dale L.
CS Dep. Mol. Exp. Med., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Bioorganic & Medicinal Chemistry Letters (1994), 4(4), 631-6
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal
LA English
AB The duocarmycins are exceptionally potent, naturally occurring antitumor antibiotics related to (+)-CC-1065. Short term exposure (1-4 h) of Molt-4 or L-1210 cells to the agents produced internucleosomal DNA fragmentation in approx. 200 base-pair multiples and at dose levels as low as 100 pM produced morphol. changes characteristic of programmed cell death. These results were associated with strong inhibition of suspension culture growth and clonogenic survival, suggesting that at phys. relevant concns., the agents induced cell death by target cell activated pathway. Presumably, this is the consequence of the sequence selective alkylation of DNA by the duocarmycins potentially at internucleosomal sites, followed by intracellular signaling with activation of endonucleases, to trigger the apoptotic cell death mechanism.
- IT **118292-36-7, (+)-Duocarmycin C2**
RL: BIOL (Biological study)
(apoptosis and endonucleolytic DNA fragmentation from, antitumor activity in relation to)
- RN 118292-36-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- L10 ANSWER 87 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:315371 CAPLUS Full-text
DN 120:315371
TI Characteristics of antitumor activity of KW-2189, a novel water-soluble derivative of duocarmycin, against murine and human tumors
AU Kobayashi, Eiji; Okamoto, Akihiko; Asada, Masao; Okabe, Masami; Nagamura, Satoru; Asai, Akira; Saito, Hiromitsu; Gomi, Katsushige; Hirata, Tadashi
CS Pharm. Res. Lab., Kyowa Hokko Kogyo Co., Ltd., Nagaizumi, 411, Japan
SO Cancer Research (1994), 54(9), 2404-10
CODEN: CNREA8; ISSN: 0008-5472
DT Journal

LA English
GI



AB KW-2189 (I), a novel derivative of duocarmycin B2, was selected for extensive evaluation based on its improved antitumor activity, water solubility, and stability in the culture medium, as compared with duocarmycin B2. Although the in vitro cell growth-inhibitory activity of KW-2189 was less potent than that of duocarmycin B2, it significantly inhibited the growth of five murine solid tumors including Colon 26 adenocarcinoma, Colon 38 adenocarcinoma, and B16 melanoma in vivo. KW-2189 was also effective against murine P388 leukemia and L1210 leukemia not only by local administration (i.p.-i.p. system), but also by systemic administration (i.p.-i.v. or i.v.-i.v. system). The most remarkable feature of KW-2189 was its efficacy against various human xenografts, which was observed in 14 tumors among 16 tested tumors including drug-insensitive tumors by single i.v. administration. Tumor regression was observed in mice bearing LC-6 lung, St-4 and St-40 stomach, Li-7 liver, PAN-2 pancreas, and MX-1 breast carcinomas. In many cases, the activities of KW-2189 were more than those of clin. active agents, mitomycin C, Adriamycin, cisplatin, and cyclophosphamide. Delayed lethal toxicity, which was reported in mice treated with CC-1065 whose structure was similar to KW-2189, was not observed in mice treated with KW-2189. KW-2189 inhibited DNA synthesis more significantly than RNA or protein synthesis, although DNA strand breaks were not observed. KW-2189 was activated by porcine liver esterase, mouse liver homogenate or Hep G2 homogenate, and DU-86-DNA adducts were detected in KW-2189-treated HeLa S3 cells, suggesting that KW-2189 was converted to DU-86 in the cells. These results indicate that KW-2189 is an interesting candidate for further development as a novel antitumor agent.

IT 154889-68-6, KW 2189

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES

(Uses)

(antitumor activity of, in human and laboratory animal)

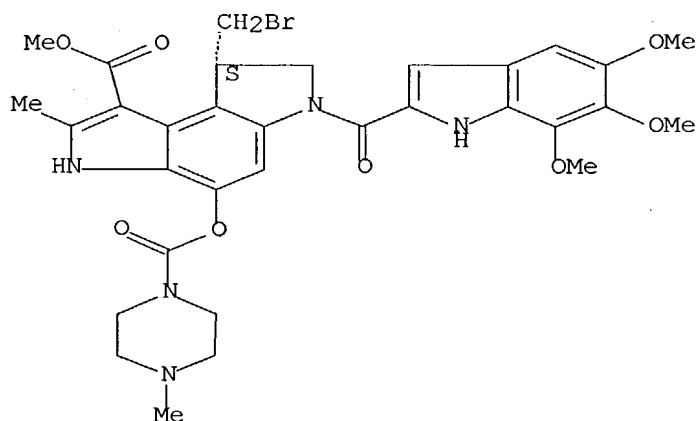
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



IT 124325-94-6, Duocarmycin B2

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES

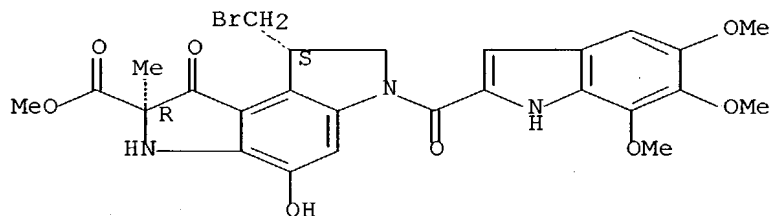
(Uses)

(antitumor activity of, in human and laboratory animal, KW-2189
comparison
with)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 88 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:315183 CAPLUS Full-text

DN 120:315183

TI A Novel Property of Duocarmycin and Its Analogs for Covalent Reaction
with

DNA

AU Asai, Akira; Nagamura, Satoru; Saito, Hiromitsu

CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Machida, 194,

Japan

SO Journal of the American Chemical Society (1994), 116(10), 4171-7
CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

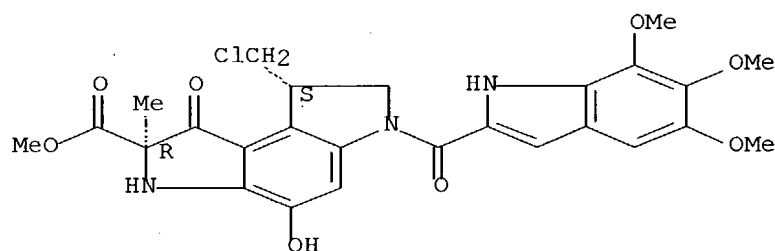
AB For understanding the mechanism of action of antitumor agents and designing new drugs, the DNA alkylating property of duocarmycin (DUM) and its analogs was examined. The thermal depurination products of calf thymus DNA covalently bonded to DUMA were revealed to be not only the DUMA-N3 adenine adduct but also unexpectedly the DUMA-N3 guanine adduct. In addition DUMSA and 2 synthetic analogs with higher solvolytic stability, reacted more selectively with N3 adenine than DUMA did. The correlation between electrophilicity of the cyclopropanesubunit in the mol. and selectivity to adenine was observed. KW-2189, a synthetic derivative which has improved in vivo antitumor activity, was designed as a prodrug requiring enzymic hydrolysis of the carbamoyl moiety, followed by the drug regeneration. Surprisingly the authors discovered that KW-2189 itself alkylated DNA covalently without release of the carbamoyl moiety. For the mechanism of DNA alkylation by KW-2189, a novel alkylating reaction via the formation of an iminium intermediate without loss of the carbamoyl moiety was proposed.

IT **118292-36-7 124325-94-6 154889-68-6**, KW 2189
RL: PRP (Properties)
(DNA alkylating property of, structure effect on)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

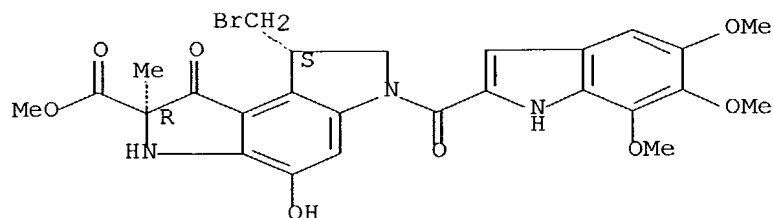
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



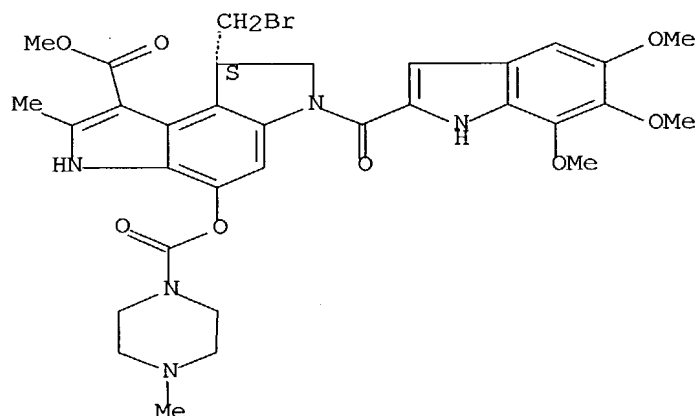
RN 154889-68-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA

INDEX

NAME)

Absolute stereochemistry.



IT 134781-55-8 150429-53-1 153212-69-2

154715-63-6 154715-64-7 154715-66-9

154715-67-0 154715-68-1 154901-65-2

RL: FORM (Formation, nonpreparative)

(formation of, antitumor activity in relation to)

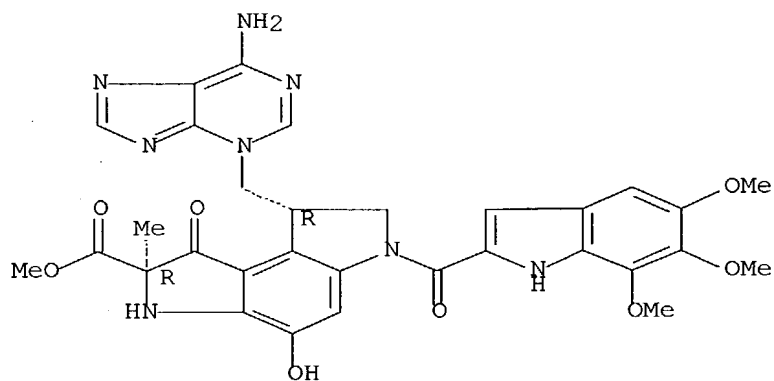
RN 134781-55-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(6-amino-3H-purin-3-yl)methyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI)

(CA

INDEX NAME)

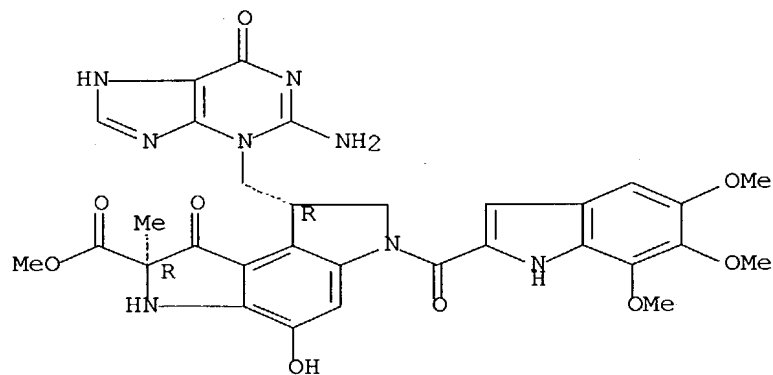
Absolute stereochemistry.



RN 150429-53-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(2-amino-6,9-dihydro-6-oxo-3H-purin-3-yl)methyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-(9CI) (CA INDEX NAME)

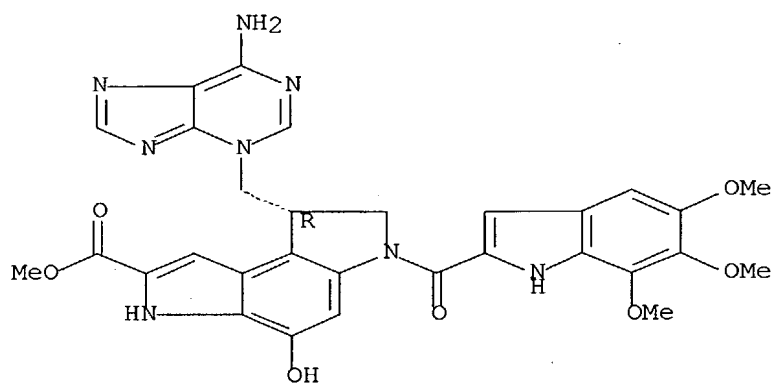
Absolute stereochemistry.



RN 153212-69-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(6-amino-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (R)-(9CI) (CA INDEX NAME)

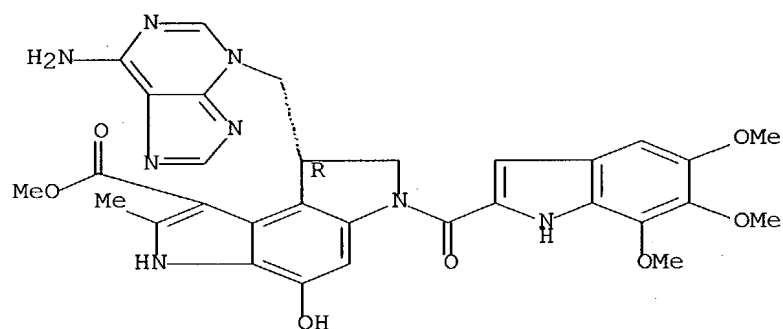
Absolute stereochemistry.



RN 154715-63-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-[(6-amino-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (R)- (9CI) (CA INDEX NAME)

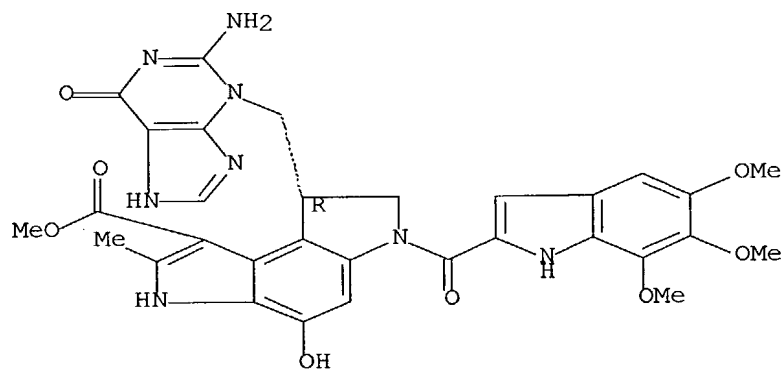
Absolute stereochemistry.



RN 154715-64-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-[(2-amino-6,7-dihydro-6-oxo-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (R)- (9CI) (CA INDEX NAME)

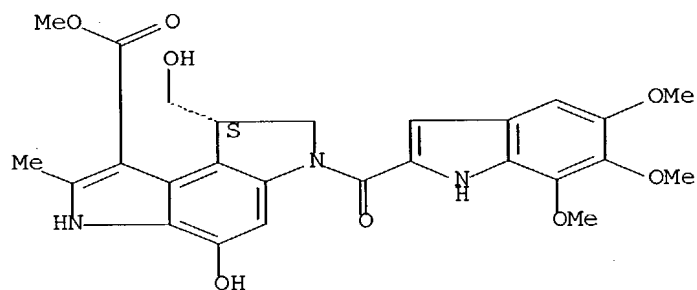
Absolute stereochemistry.



RN 154715-66-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-4-hydroxy-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

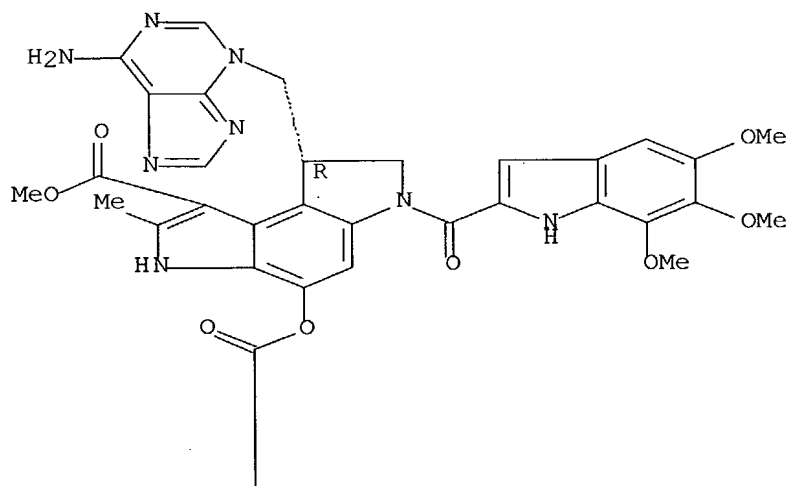


RN 154715-67-0 CAPLUS

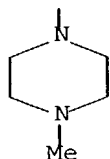
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-[(6-amino-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

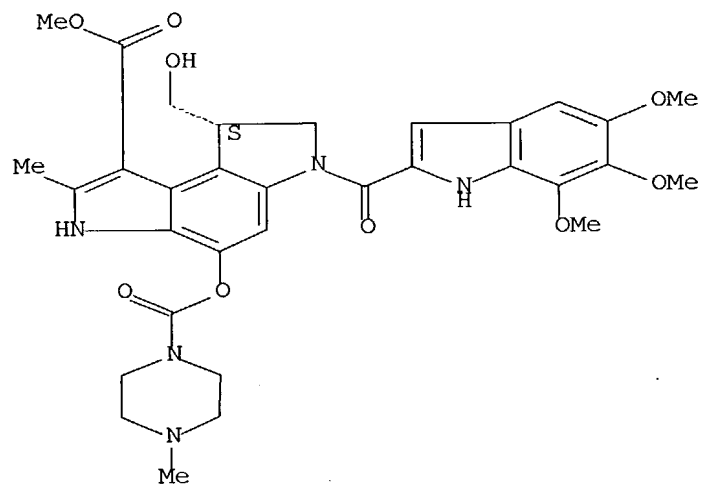


PAGE 2-A



RN 154715-68-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, (S)- (9CI)
(CA INDEX NAME)

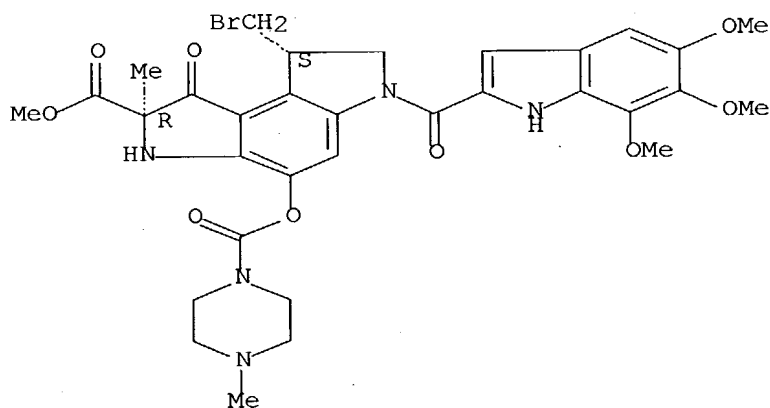
Absolute stereochemistry.



RN 154901-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-
piperazinyl) carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester,
(2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 89 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:260557 CAPLUS Full-text

DN 120:260557

TI Interconversion and stability of duocarmycins, a new family of antitumor
antibiotics: correlation to their cytotoxic and antimicrobial activities
in vitro

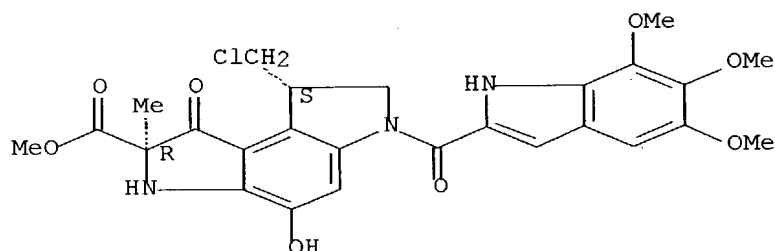
AU Ichimura, Michio; Ogawa, Tatsuhiro; Takahashi, Keiichi; Mihara, Akira;

Takahashi, Isami; Nakano, Hirofumi
 CS Pharm. Res. Lab., Kyowa Hakko Co., Ltd., Machida, 194, Japan
 SO Oncology Research (1993), 5(4-5), 165-71
 CODEN: ONREE8; ISSN: 0965-0407
 DT Journal
 LA English
 AB Stability and interconversion of duocarmycins were studied in relation to their cytotoxicities and antimicrobial activities. The compds. studied included duocarmycin A and SA, which have a spirocyclopropylhexadienone moiety, and four halogenated seco-compds. of duocarmycin A: duocarmycin B1, B2, C1 and C2, from which the cyclopropane ring structure is absent. Duocarmycins were potent cytotoxic compds. to cells. The cytotoxic activity seen on Balb 3T3/H-ras cells after 72 h drug exposure was in the following order (IC50 (nM): concentration for 50% growth inhibition); SA (0.05) > A (0.3) > B2 (1.5) > B1 (3.0) > C2 (20) > C1 (40). Average min. inhibitory concns. (MICs) of duocarmycins against microorganisms showed essentially the same ranking order as that of cytotoxicity. There was a large difference between SA and A in their stability in aqueous solvents. For halogenated seco-compds., a good correlation was found between their cytotoxicities in vitro and their conversion rate to duocarmycin A, suggesting that halogenated seco-compds. undergo closure to the spirocyclopropylhexadienone structure, the pertinent active form, in cells.

IT **118292-36-7**, Duocarmycin C2 **124325-94-6**, Duocarmycin B2
 RL: BIOL (Biological study)
 (cytotoxic and antimicrobial activities of, interconversion and stability of duocarmycins in relation to)

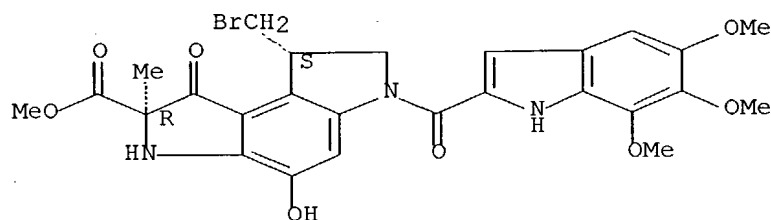
RN 118292-36-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



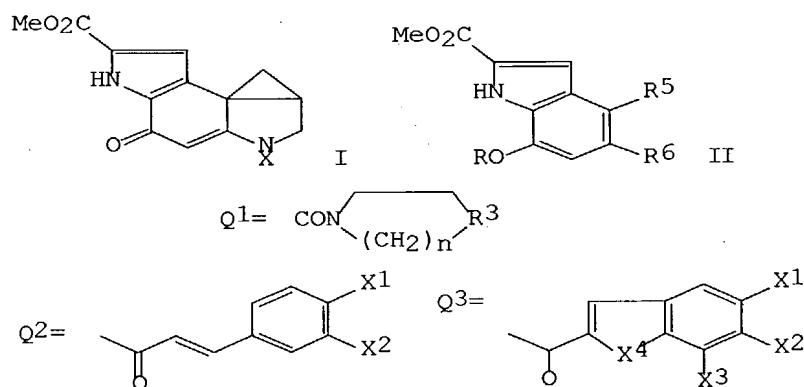
RN 124325-94-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 90 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:163825 CAPLUS Full-text
 DN 120:163825
 TI Preparation of DC 113 derivatives as antitumor or antimicrobial agents
 IN Nagamura, Akihito; Saito, Hiromitsu; Ogawa, Tatsuhiro; Katsumata, Shigeo;
 Mihara, Akira; Takahashi, Keiichi; Kobayashi, Eiji; Gomi, Katsunari
 PA Kyowa Hakko Kogyo Kk, Japan
 SO Jpn. Kokai Tokkyo Koho, 15 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 05208979	A2	19930820	JP 1992-153534	19920612
PRAI	JP 1991-158897		19910628		
OS	MARPAT 120:163825				
GI					



AB The title compds. I, II [R = H, CONR₁R₂, Q₁; R₁, R₂ = H, lower alkyl; R₃ = CH₂, O, NMe; R₅R₆ = CH(CH₂Z)CH₂NX, CH₂CH(CH₂Z)CH₂NX; X = H, Q₂, Q₃; X₁-3 = H, OR₄; X₄ = NH, O; R₄ = lower alkyl; Z = Cl, Br; n = 0-4; if X in I = Q₃ and X₄ = NH, then X₁, X₂, and/or X₃ = H], or their salts are

prepared DC 113 in MeCN was treated with HCl at room temperature for 1 h and the reaction product was treated with p-nitrophenyl chloroformate and NEt₃ in CH₂Cl₂ at -50° for 0.5 h followed by Me₂NH at -50° to room temperature for 0.5 h to give 57% II (R = CONMe₂, R₅R₆ = CH(CH₂Cl)CH₂NX, X = Q₃, X₁-3 = OMe, X₄ = NH), which inhibited growth of HeLaS3 cells with IC₅₀ of 0.78 nM.

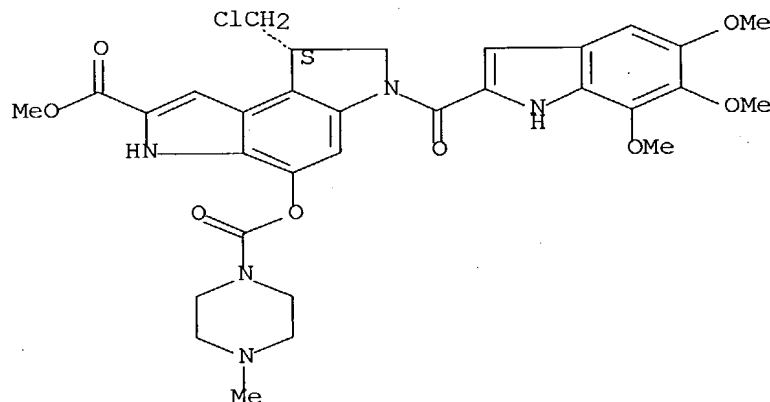
IT 152718-02-0P 152718-03-1P 152718-04-2P
152718-05-3P 152718-07-5P 152718-08-6P
152718-09-7P 152718-10-0P 152718-11-1P
152785-82-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antitumor and antimicrobial agent)

RN 152718-02-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-
trimethoxy-
1H-indol-2-yl) carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

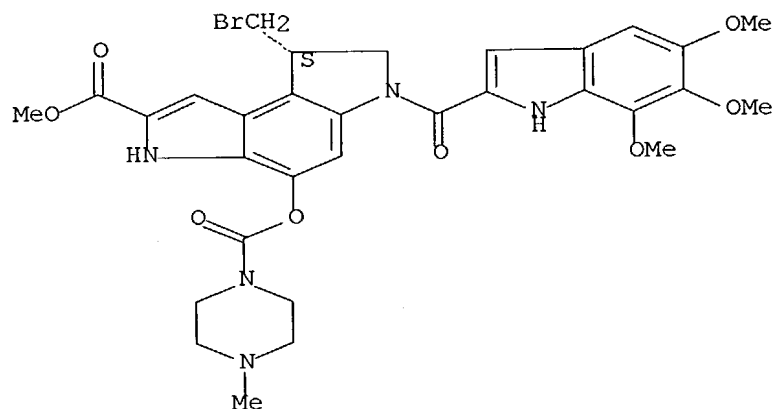
Absolute stereochemistry.



RN 152718-03-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-
trimethoxy-
1H-indol-2-yl) carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

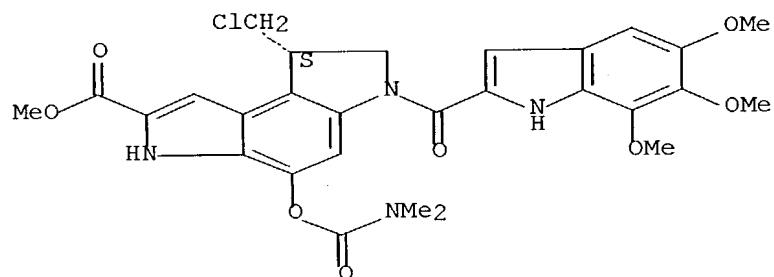


RN 152718-04-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-

1H- indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

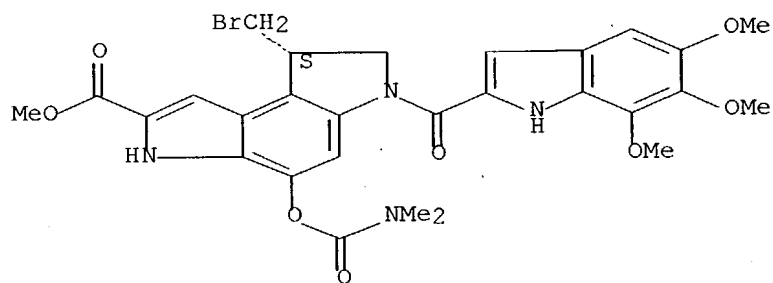


RN 152718-05-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-

1H- indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

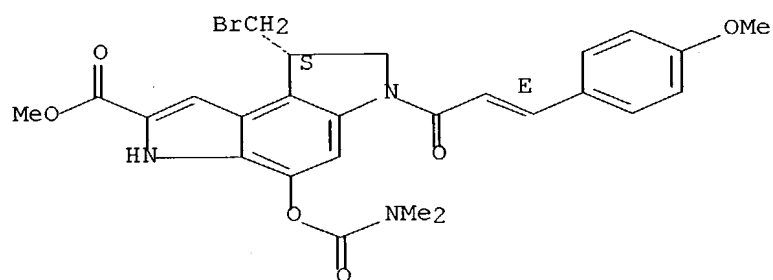


RN 152718-07-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(dimethylamino) carbonyl] oxy]-3,6,7,8-tetrahydro-6-[3-(4-
 methoxyphenyl)-1-
 oxo-2-propenyl]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

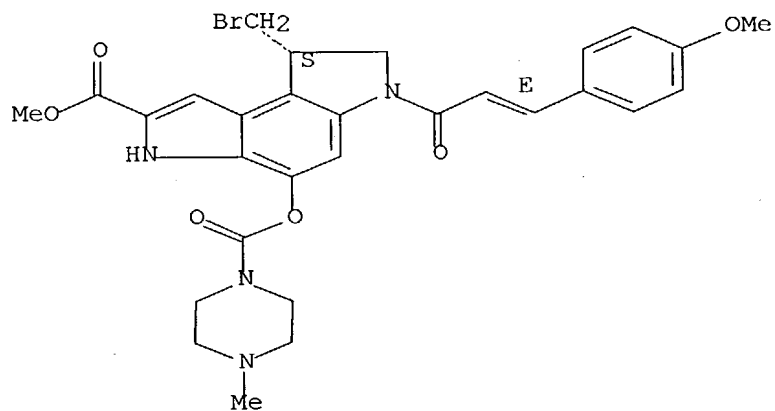


RN 152718-08-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
 tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[(4-methyl-1-
 piperazinyl) carbonyl] oxy]-, methyl ester, [S-(E)]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

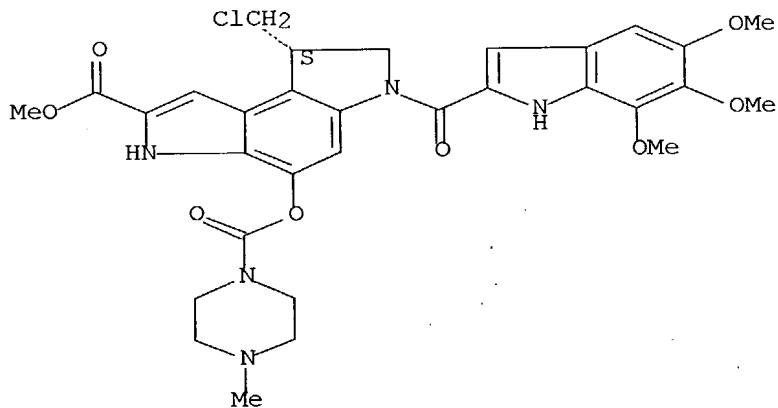
Double bond geometry as shown.



RN 152718-09-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-
 trimethoxy-
 1H-indol-2-yl) carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

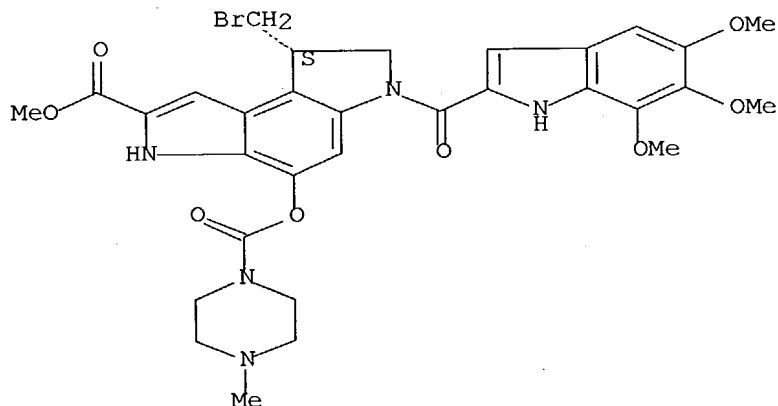
● HCl

RN 152718-10-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

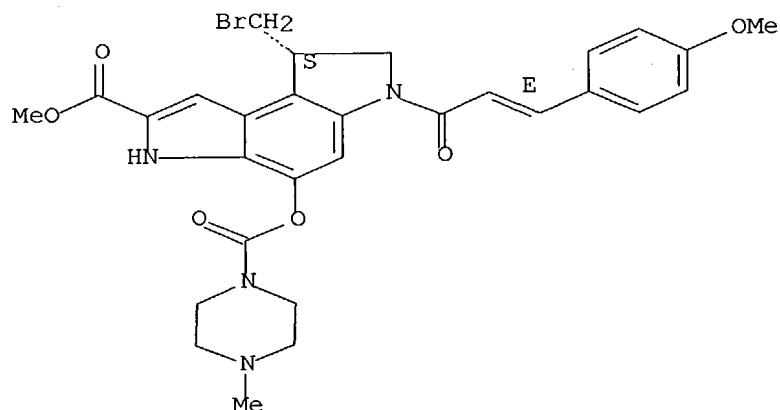


PAGE 2-A

● HCl

RN 152718-11-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-, methyl ester, monohydrochloride, [S-(E)]-(9CI) (CA INDEX NAME)

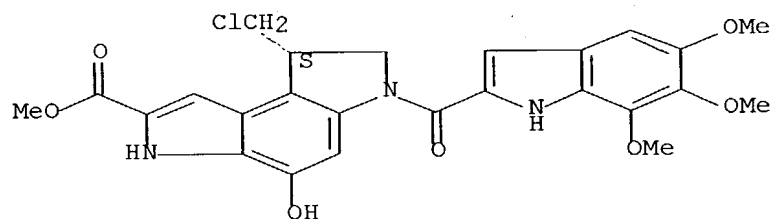
Absolute stereochemistry.
Double bond geometry as shown.



● HCl

RN 152785-82-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl
 ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 91 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1994:153162 CAPLUS Full-text
 DN 120:153162
 TI (+)- and ent-(-)-Duocarmycin SA and (+)- and ent-(-)-N-BOC-DSA DNA
 Alkylation Properties. Alkylation Site Models That Accommodate the Offset
 AT-Rich Adenine N3 Alkylation Selectivity of the Enantiomeric Agents
 AU Boger, Dale L.; Johnson, Douglas S.; Yun, Weiya
 CS Department of Chemistry, The Scripps Research Institute, La Jolla, CA,

92037, USA

SO Journal of the American Chemical Society (1994), 116(5), 1635-56
CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

AB A detailed study of the DNA alkylation properties of (+)-duocarmycin SA, ent-(-)-duocarmycin SA, and (+)- and ent-(-)-N-BOC-DSA is described, and the development of a model that accommodates the offset AT-rich adenine N3 alkylation selectivity of the enantiomeric agents is presented.

IT 153212-69-2 153212-70-5

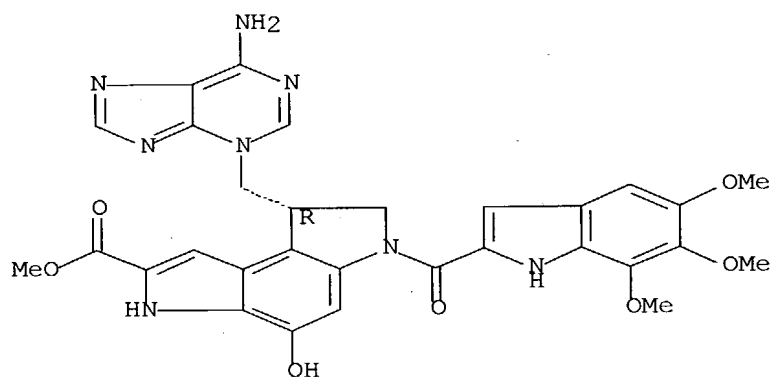
RL: PROC (Process)

(isolation of, in duocarmycin SA binding to DNA)

RN 153212-69-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(6-amino-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (R)- (9CI) (CA INDEX NAME)

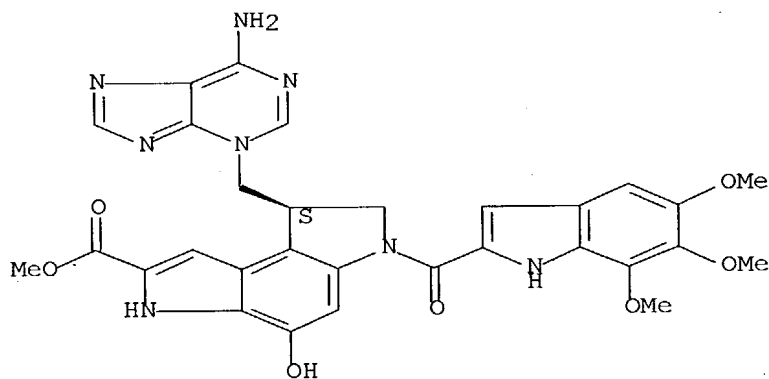
Absolute stereochemistry.



RN 153212-70-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(6-amino-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 92 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:649750 CAPLUS Full-text

DN 119:249750

TI Total synthesis and preliminary evaluation of (+)- and ent-(-)-duocarmycin

SA

AU Boger, Dale L.; Machiya, Kozo; Hertzog, Donald L.; Kitos, Paul A.; Holmes, Daniel

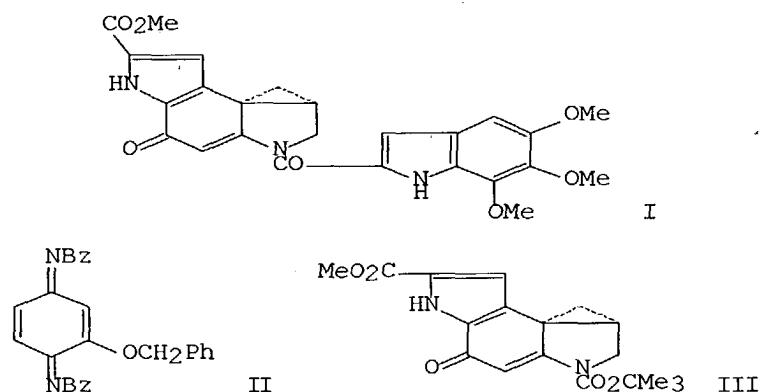
CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA

SO Journal of the American Chemical Society (1993), 115(20), 9025-36
CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

GI



AB Concise total syntheses of natural (+)- (I) and ent-(-)-duocarmycin SA are based on sequential regioselective nucleophilic substitution reactions of the unsym. p-quinonediimine II in the preparation of a dihydropyrroloindole precursor to the left-hand subunit. In addition to constituting a new synthetic strategy for the preparation of I and related agents, both enantiomers of N-BOC-DSA (III) and its immediate synthetic precursors are made available by the approach. This provides access to synthetic analogs incorporating either enantiomer of the exceptionally stable and potent duocarmycin SA alkylation subunit. Studies reveal that III is 4.8 times more stable to chemical solvolysis than N-BOC-CPI, the authentic alkylation subunit of CC-1065, and that the agents participate in a stereoelectronically-controlled solvolysis reaction with nucleophilic addition to the least hindered cyclopropane carbon. Consistent with this enhanced stability, (+)-III had the most potent inherent cytotoxic activity of all natural and synthetic alkylation subunits examined to date including (+)-N-BOC-CPI, and its relative cytotoxic potency predictably follows a fundamental

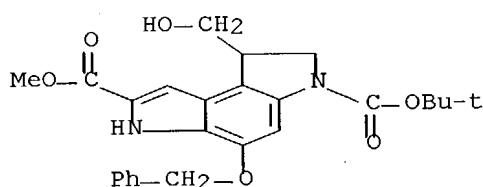
relationship between chemical stability and cytotoxic potency established in prior studies. In contrast to expectations based on past observations, the unnatural enantiomers of I and III also constituted potent cytotoxic agents whose further examination should prove exceptionally interesting.

IT 144667-35-6P 144667-36-7P 144667-37-8P
144667-38-9P 144667-39-0P 144732-54-7P
144732-55-8P 144732-56-9P 144786-07-2P
151062-85-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate in preparation of duocarmycin SA)

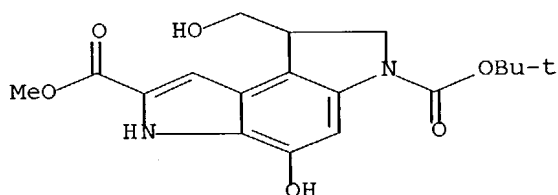
RN 144667-35-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester (9CI) (CA INDEX NAME)



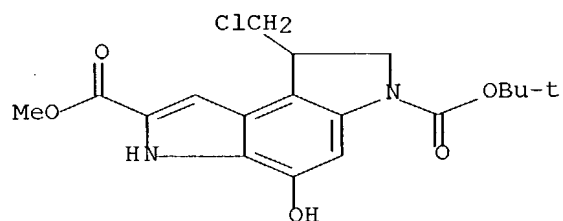
RN 144667-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
7,8-dihydro-4-hydroxy-8-(hydroxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl
ester (9CI) (CA INDEX NAME)

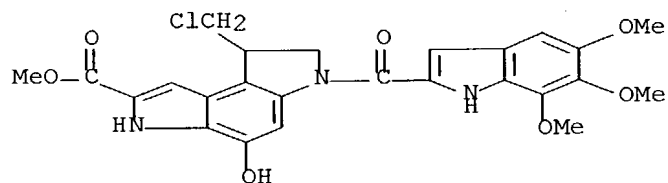


RN 144667-37-8 CAPLUS

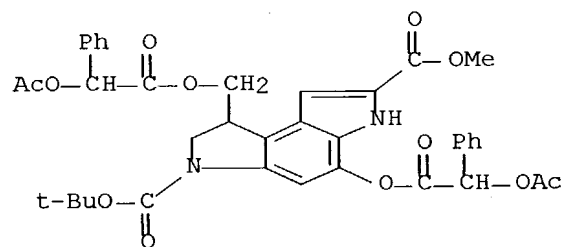
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester (9CI) (CA INDEX NAME)



RN 144667-38-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl
 ester (9CI) (CA INDEX NAME)

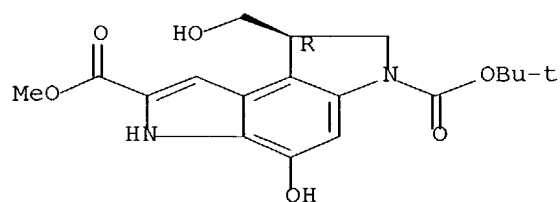


RN 144667-39-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 4-[[[(acetyloxy)phenylacetyl]oxy]-8-
 [[[acetyloxy)phenylacetyl]oxy]methyl]-
 7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester, [8R-
 [4(R*), 8R*(R*)]]-
 (9CI) (CA INDEX NAME)



RN 144732-54-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid,
 1,6-dihydro-5-hydroxy-1-(hydroxymethyl)-, 3-(1,1-dimethylethyl) 7-methyl
 ester, (R)- (9CI) (CA INDEX NAME)

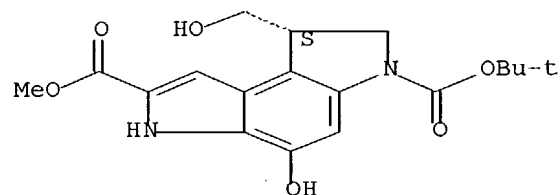
Absolute stereochemistry.



RN 144732-55-8 CAPLUS

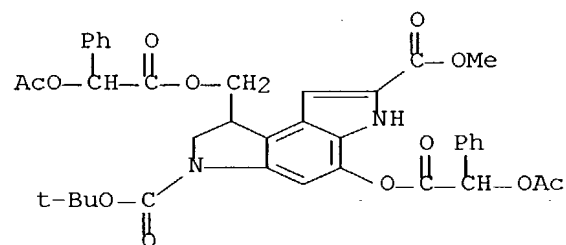
CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid,
1,6-dihydro-5-hydroxy-1-(hydroxymethyl)-, 3-(1,1-dimethylethyl) 7-methyl
ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144732-56-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
4-[[[(acetyloxy)phenylacetyl]oxy]-8-
[[[(acetyloxy)phenylacetyl]oxy]methyl]-
7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester, [8S-
[4(S*),8R*(S*)]]-
(9CI) (CA INDEX NAME)

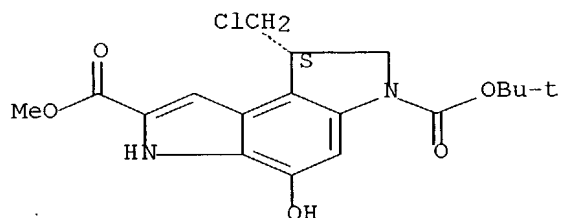


RN 144786-07-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl

ester, (8S)- (9CI) (CA INDEX NAME)

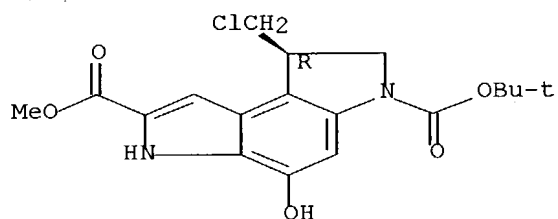
Absolute stereochemistry. Rotation (-).



RN 151062-85-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



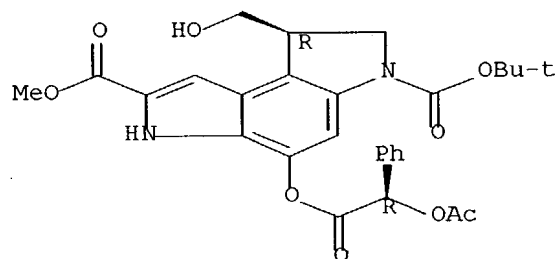
IT 150992-78-2P 150992-79-3P 150992-80-6P
150992-81-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 150992-78-2 CAPLUS

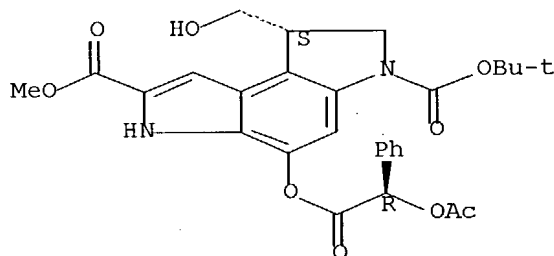
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
4-[[[acetyloxy]phenylacetyl]oxy]-7,8-dihydro-8-(hydroxymethyl)-,
6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,R*)]- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



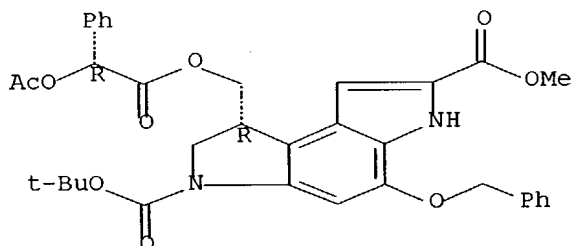
RN 150992-79-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 4-[[[(acetyloxy)phenylacetyl]oxy]-7,8-dihydro-8-(hydroxymethyl)-,
 6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,S*)]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.



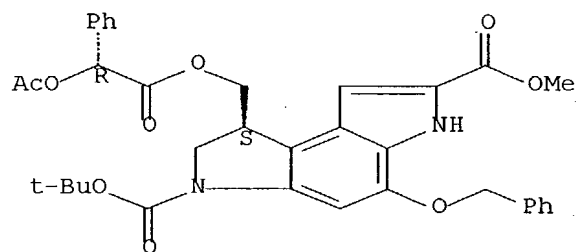
RN 150992-80-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-,
 6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,R*)]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.



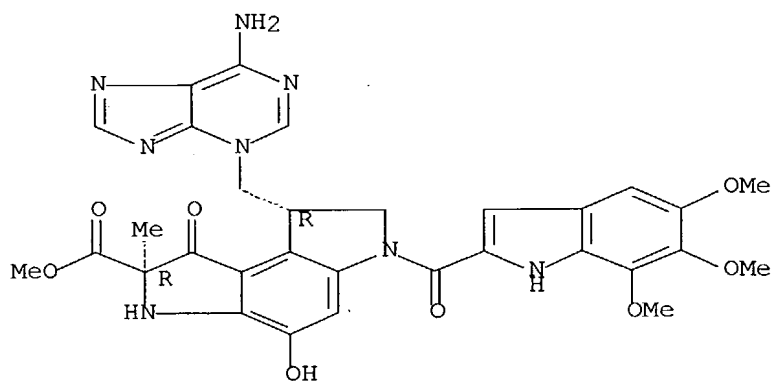
RN 150992-81-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-,
 6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,S*)]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.



L10 ANSWER 93 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:603748 CAPLUS Full-text
 DN 119:203748
 TI A novel guanine N3 alkylation by antitumor antibiotic duocarmycin A
 AU Sugiyama, Hiroshi; Ohmori, Kazushige; Chan, Kit Lam; Hosoda, Masahiro;
 Asai, Akira; Saito, Hiromitsu; Saito, Isao
 CS Fac. Eng., Kyoto Univ., Kyoto, 606, Japan
 SO Tetrahedron Letters (1993), 34(13), 2179-82
 CODEN: TELEAY; ISSN: 0040-4039
 DT Journal
 LA English
 AB Antitumor antibiotic duocarmycin A was found to undergo a novel N3
 alkylation of the guanine residue (G7) of d(GCAATTGC)2. Guanine base
 was shown to be a second major target of duocarmycin A in DNA.
 IT **150429-49-5P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT
 (Reactant or reagent)
 (preparation and thermolysis of)
 RN 150429-49-5 CAPLUS
 CN Cytidine, 2'-deoxyguanylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-
 2'-deoxyadenylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-
 (3'→5')-thymidylyl-(3'→5')-2'-deoxy-3-[[(1R,7R)-1,2,3,6,7,8-
 hexahydro-5-hydroxy-7-(methoxycarbonyl)-7-methyl-8-oxo-3-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-1-
 yl)methyl]guanylyl-(3'→5')-2'-deoxy- (9CI) (CA INDEX NAME)
 *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 IT **134781-55-8P 150429-50-8P 150429-52-0P**
150429-53-1P 150464-11-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 134781-55-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(6-amino-3H-purin-3-
 yl)methyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI)
 (CA
 INDEX NAME)

Absolute stereochemistry.



RN 150429-50-8 CAPLUS
 CN Cytidine, 2'-deoxyguanylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-
 2'-deoxyadenylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-
 (3'→5')-thymidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-
 2'-deoxy-, complex with 2'-deoxyguanylyl-(3'→5')-2'-deoxycytidylyl-
 (3'→5')-2'-deoxyadenylyl-(3'→5')-2'-deoxyadenylyl-
 (3'→5')-thymidylyl-(3'→5')-thymidylyl-(3'→5')-2'-
 deoxy-3-[[[(1R,7R)-1,2,3,6,7,8-hexahydro-5-hydroxy-7-(methoxycarbonyl)-7-
 methyl-8-oxo-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-
 b:4,3-
 b']dipyrrol-1-yl)methyl]guanylyl-(3'→5')-2'-deoxycytidine (1:1)
 (9CI) (CA INDEX NAME)

CM 1

CRN 150429-49-5
 CMF C104 H124 N33 O54 P7

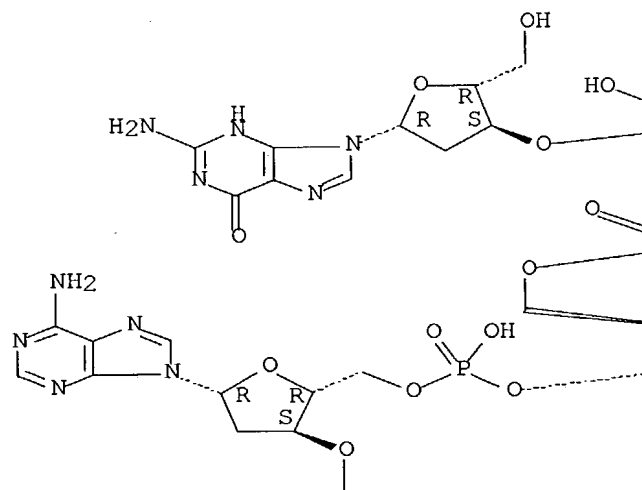
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

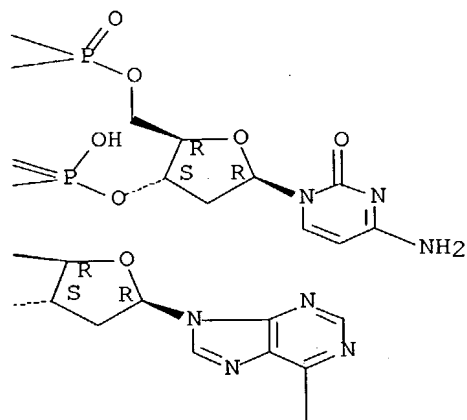
CRN 127761-90-4
 CMF C78 H99 N30 O46 P7

Absolute stereochemistry.

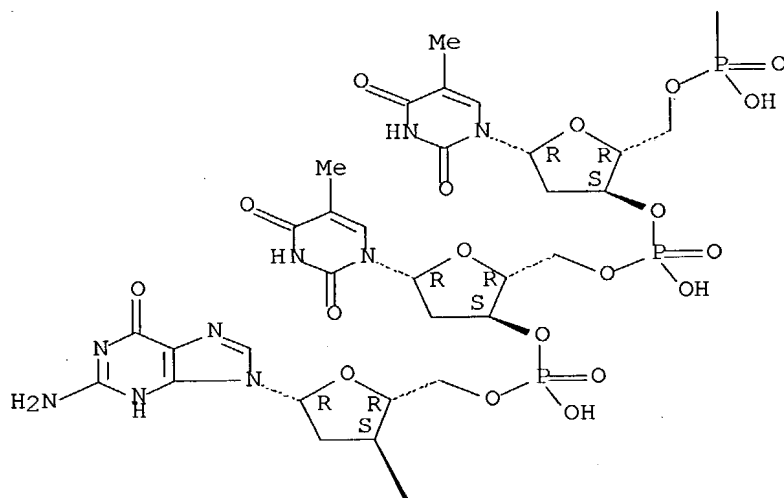
PAGE 1-A



PAGE 1-B



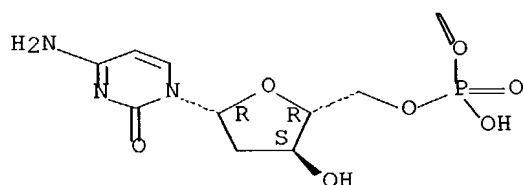
PAGE 2-A



PAGE 2-B



PAGE 3-A



RN 150429-52-0 CAPLUS

CN Guanosine, 2'-deoxycytidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxy-, complex with (1R-trans)-2'-deoxycytidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxy-3-[[1,2,3,6,7,8-hexahydro-5-hydroxy-7-(methoxycarbonyl)-7-methyl-8-oxo-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl]guanylyl-(3'→5')-2'-deoxycytidylyl-

(3'→5')-2'-deoxyguanosine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 150429-51-9

CMF C104 H124 N33 O54 P7

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

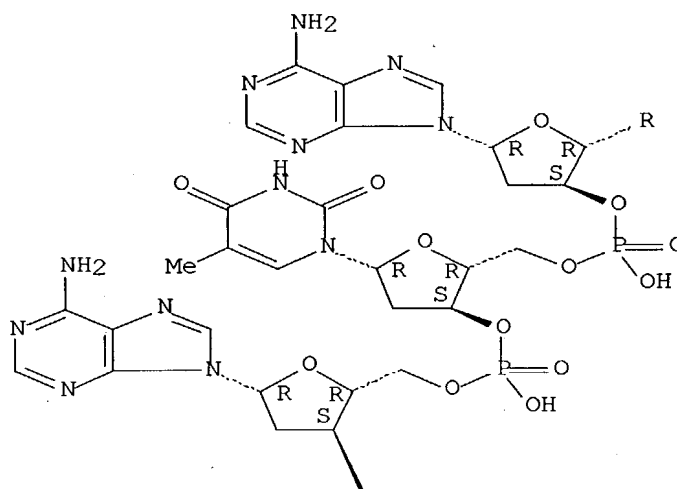
CM 2

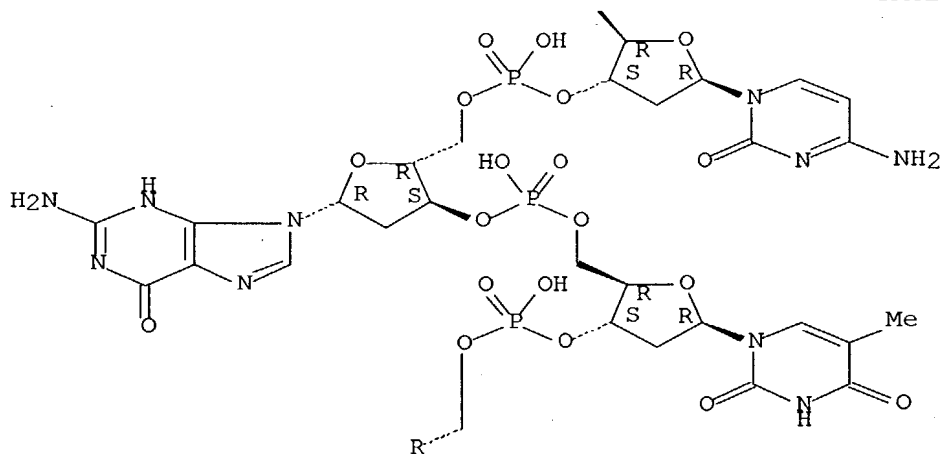
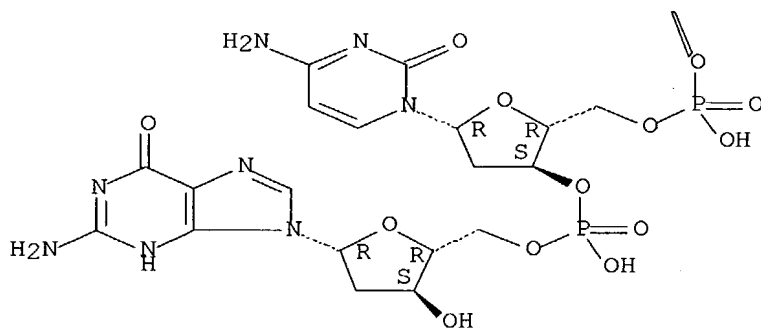
CRN 132930-28-0

CMF C78 H99 N30 O46 P7

Absolute stereochemistry.

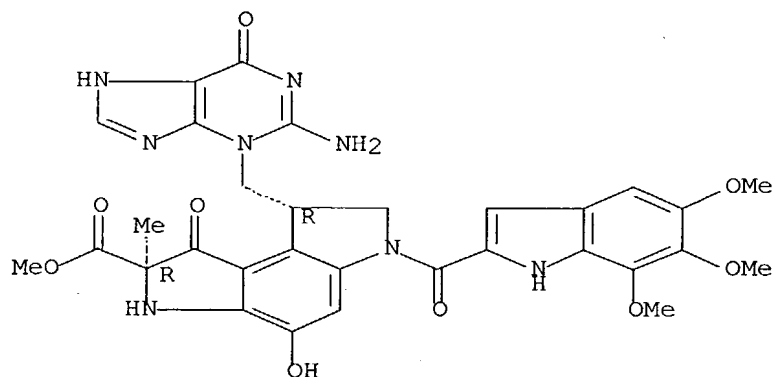
PAGE 1-A





RN 150429-53-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(2-amino-6,9-dihydro-6-oxo-3H-purin-3-yl)methyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150464-11-2 CAPLUS
 CN Cytidine, 2'-deoxyguanylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-
 2'-deoxyadenylyl-(3'→5')-thymidylyl-(3'→5')-2'-deoxyadenylyl-
 (3'→5')-thymidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-
 2'-deoxy-, complex with 2'-deoxyguanylyl-(3'→5')-2'-deoxycytidylyl-
 (3'→5')-2'-deoxyadenylyl-(3'→5')-thymidylyl-(3'→5')-
 2'-deoxy-3-[[(1R,7R)-1,2,3,6,7,8-hexahydro-5-hydroxy-7-
 (methoxycarbonyl)-7-
 methyl-8-oxo-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-
 b:4,3-
 b']dipyrrol-1-yl)methyl]adenylyl-(3'→5')-thymidylyl-(3'→5')-
 2'-deoxy-3-[[(1R,7R)-1,2,3,6,7,8-hexahydro-5-hydroxy-7-
 (methoxycarbonyl)-7-
 methyl-8-oxo-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-
 b:4,3-
 b']dipyrrol-1-yl)methyl]guanylyl-(3'→5')-2'-deoxycytidine (1:1)
 (9CI) (CA INDEX NAME)

CM 1

CRN 150464-10-1

CMF C130 H149 N36 O62 P7

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

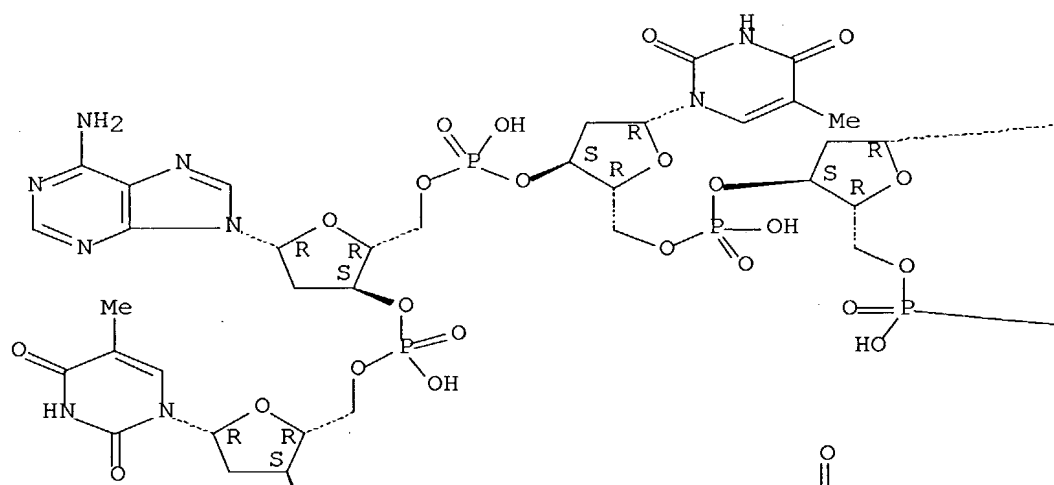
CM 2

CRN 113813-12-0

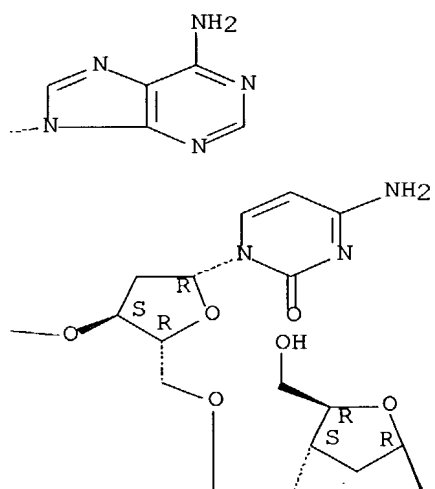
CMF C78 H99 N30 O46 P7

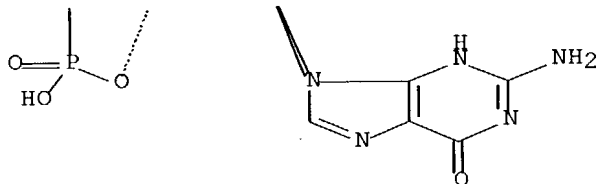
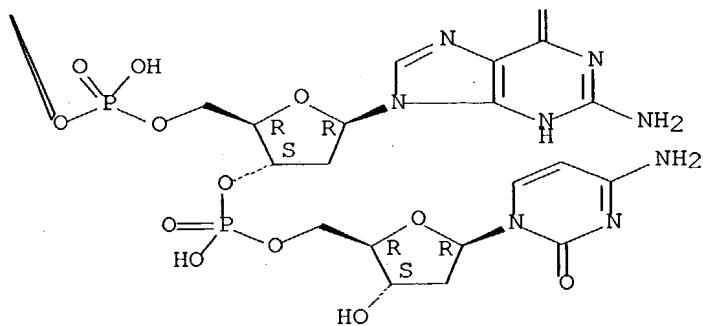
Absolute stereochemistry.

PAGE 1-A

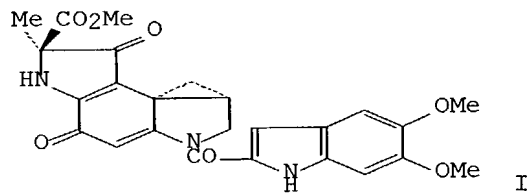


PAGE 1-B





L10 ANSWER 94 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:538951 CAPLUS Full-text
 DN 119:138951
 TI Synthesis and cytotoxicity of enantiomeric pairs of duocarmycin a and
 its
 2-epimer
 AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Terashima, Shiro
 CS Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Nogi, 329-01, Japan
 SO Bioorganic & Medicinal Chemistry Letters (1992), 2(7), 755-8
 CODEN: BMCLE8; ISSN: 0960-894X
 DT Journal
 LA English
 GI



AB The synthesis of the four possible diastereomers of duocamycin A (I) was achieved through optical resolution of a tricyclic synthetic intermediate. The stereochem. configuration of the cyclopropane ring was found to be closely related with their cytotoxicity against P388 murine leukemia.

IT **149405-53-8P 149405-54-9P 149405-56-1P**
149405-57-2P

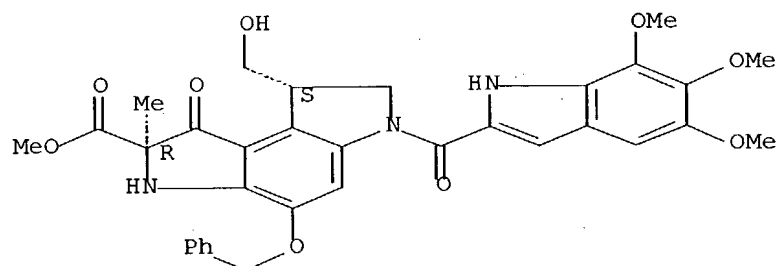
RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and conversion of, to duocarmycin)

RN 149405-53-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-

1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

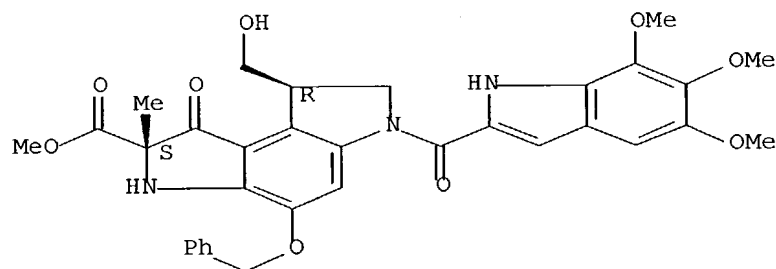


RN 149405-54-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-

1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

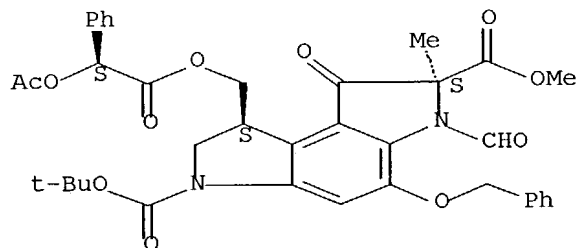


RN 149405-56-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2S-[2 α ,8 α (R*)]]- (9CI) (CA INDEX NAME)

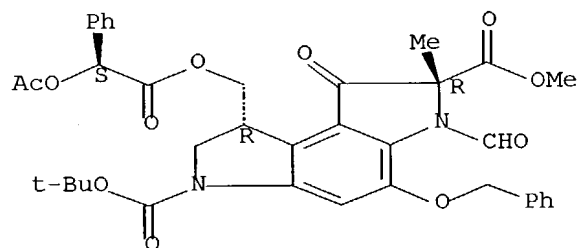
Absolute stereochemistry. Rotation (-).



RN 149405-57-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2R-[2 α ,8 α (S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 132628-67-2P 132628-68-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

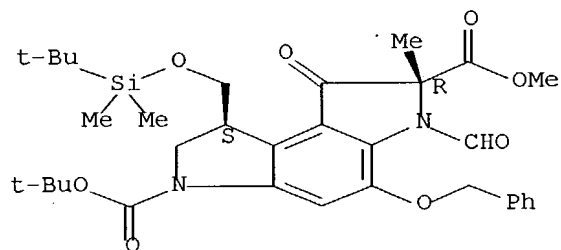
(Reactant or reagent)

(preparation and desilylation of)

RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

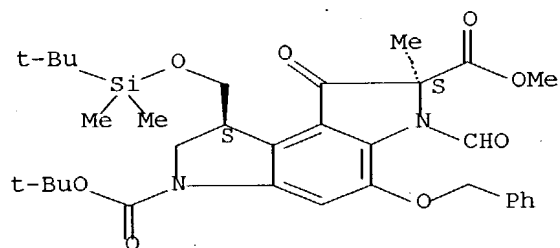
Relative stereochemistry.



RN 132628-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 149365-66-2P 149365-67-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation, acylation, and resolution of)

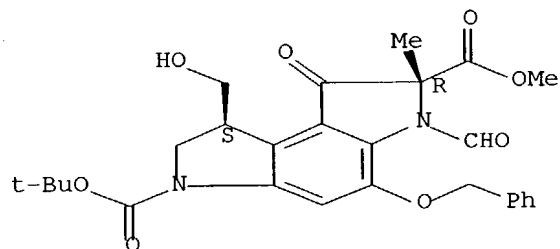
RN 149365-66-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI)

(CA

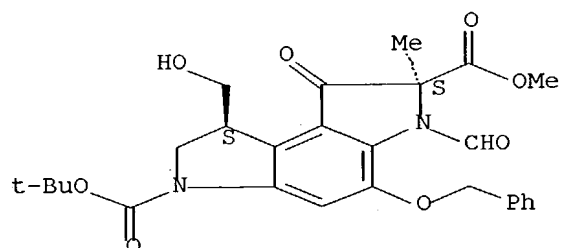
INDEX NAME)

Relative stereochemistry.



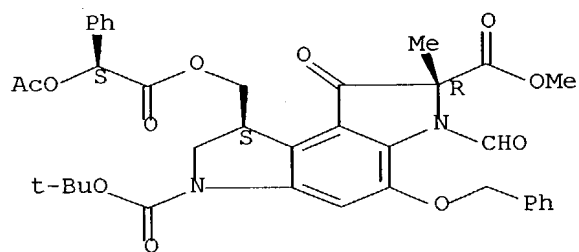
RN 149365-67-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid,
 6-formyl-1,6,7,8-tetrahydro-1-(hydroxymethyl)-7-methyl-8-oxo-5-
 (phenylmethoxy)-, 3-(1,1-dimethylethyl) 7-methyl ester, cis- (9CI) (CA
 INDEX NAME)

Relative stereochemistry.



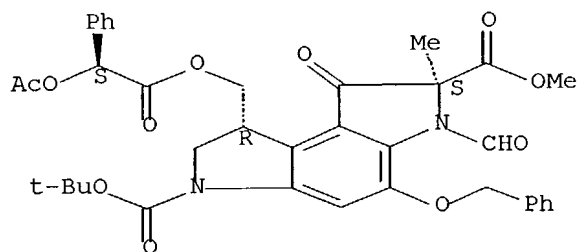
IT **149365-68-4P 149405-52-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT
 (Reactant or reagent)
 (preparation, hydrolysis, and acylation of, with indolylcarboxylate)
 RN 149365-68-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
 8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-
 methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester,
 [2R-[2 α ,8 β (S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



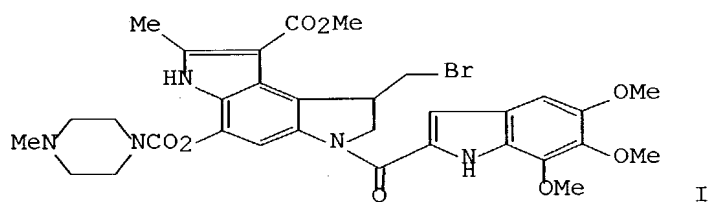
RN 149405-52-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
 8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-
 methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
 [2S-[2 α ,8 β (R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 95 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:456138 CAPLUS Full-text
 DN 119:56138
 TI Hydrobromide of antitumor DC-89 with high stability
 IN Nagamura, Satoru; Saito, Hiromitsu; Hayakawa, Eiji; Kato, Yasuki;
 Naganuma, Hirotake
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 6 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 537575	A1	19930421	EP 1992-116898	19921002
	R: DE, FR, GB, IT				
	JP 05097853	A2	19930420	JP 1991-259188	19911007
	CA 2079733	AA	19930408	CA 1992-2079733	19921002
PRAI	JP 1991-259188		19911007		
GI					



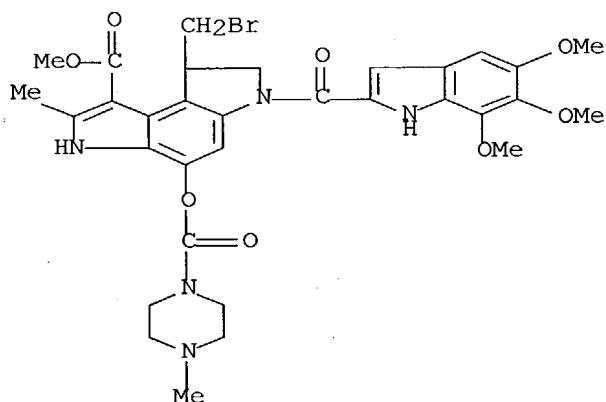
I

AB Hydrobromide of antitumor DC-89 (I) with high stability in solns. for producing freeze-dried preps. are prepared by reaction of HBr with the base. The residual rate of a solution of 1 mg I/mL at 25° after 6 h was 98 %. Antitumor activity of I against sarcoma tumor was equal to its HCl salt.
 IT **148778-32-9P**
 RL: PREP (Preparation)
 (preparation of, with high stability in solns.)

RN 148778-32-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide (9CI)

(CA INDEX NAME)



● HBr

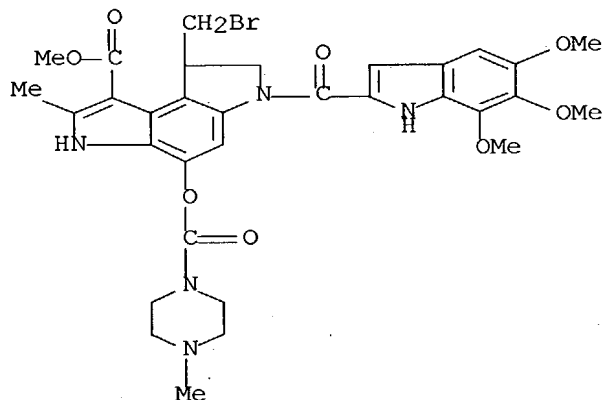
IT 134106-78-8

RL: PROC (Process)

(salt formation of, with hydrobromic acid, with high stability in solns.)

RN 134106-78-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 96 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:191718 CAPLUS Full-text

DN 118:191718
 TI Preparation of DC-89 derivatives as neoplasm inhibitors and
 antibacterials
 IN Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji; Gomi, Katsushige
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 20 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 520435	A2	19921230	EP 1992-110688	19920625
	EP 520435	A3	19930505		
	R: DE, FR, GB, IT				
	JP 05178858	A2	19930720	JP 1992-167102	19920625
	US 5258383	A	19931102	US 1992-903756	19920625
PRAI	JP 1991-158896		19910628		
OS	MARPAT 118:191718				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. (I; X = H, CO₂Me; Q = Q1, Q2; W = H, Q3; W1, W2 = H, OR4;
 R4 = alkyl, alkenyl; Z = Cl, Br; R = H, carbamoyl), were prepared. Thus,
 precursor II was N-deacylated with NaOMe in MeOH (99% yield) and the
 product was condensed with 4-nitrophenyl 4-methoxycinnamate using NaH in
 DMF (85% yield). The cinnamide was stirred with 48% HBr in MeCN to give
 a residue which in CH₂Cl₂ was treated sequentially p-nitrophenyl
 chloroformate, Et₃N, and aq- Me₂NH to give 90% title compound III. III
 at 8.0 mg/kg i.v. in mice implanted with sarcoma 180 tumors reduced
 tumor volume to 2-7% of the volume of untreated controls.

IT **146940-80-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

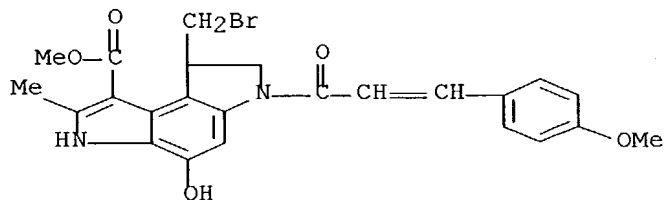
RACT

(Reactant or reagent)

(preparation and carbamoylation of, in preparation of neoplasm
inhibitor)

RN 146940-80-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
 tetrahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-,
 methyl ester (9CI) (CA INDEX NAME)

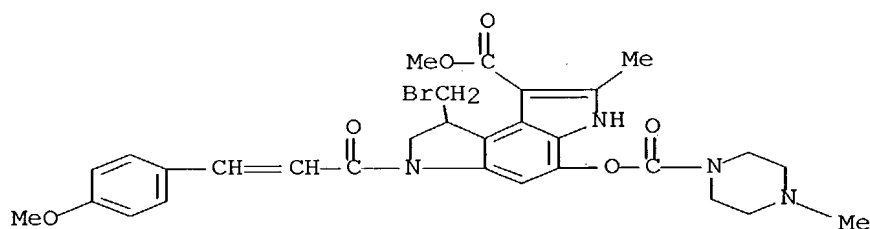


IT 146910-07-8P 146910-08-9P 146910-09-0P
 146940-70-7P 146940-71-8P 146940-72-9P
 146940-73-0P 146940-74-1P 146940-75-2P
 146940-76-3P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as neoplasm inhibitor)

RN 146910-07-8 CAPLUS

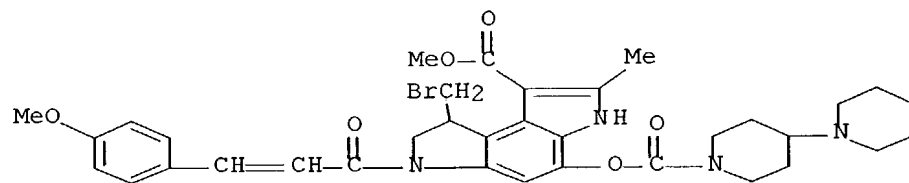
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 146910-08-9 CAPLUS

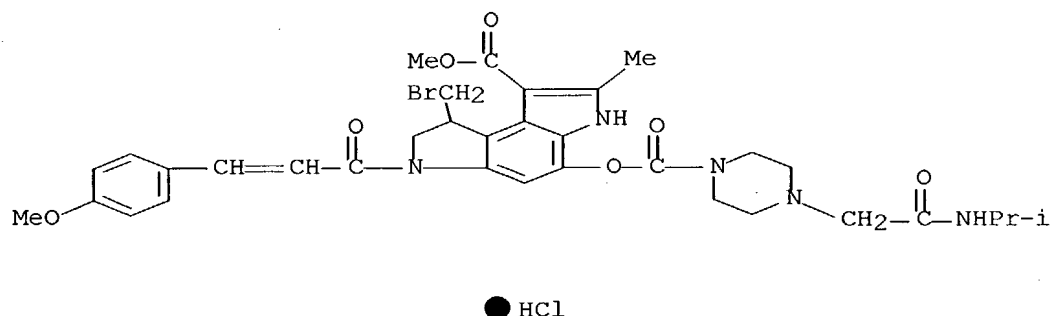
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-ylcarbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

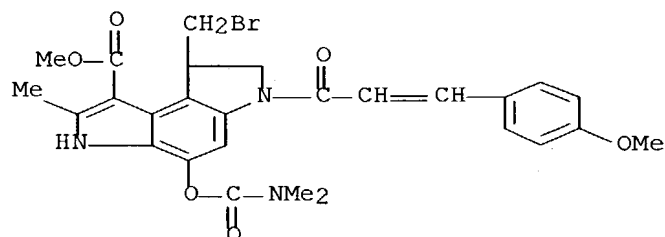
RN 146910-09-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-(2-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



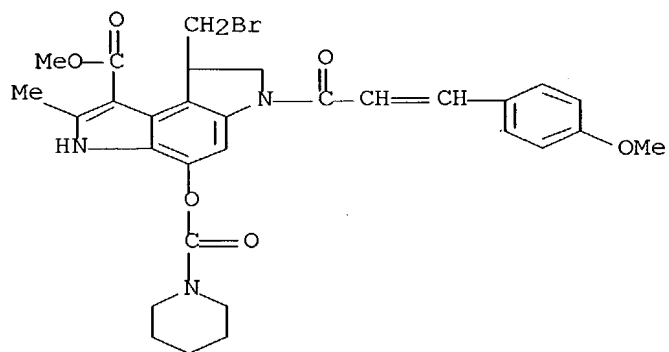
RN 146940-70-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino) carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



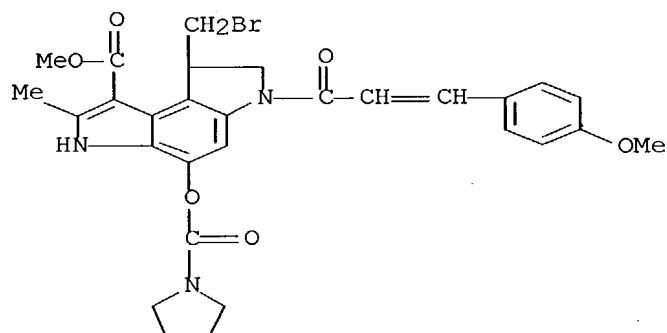
RN 146940-71-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



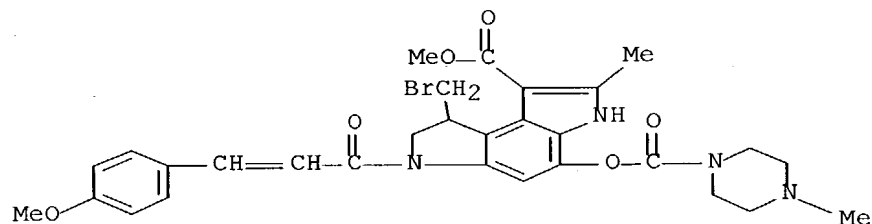
RN 146940-72-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



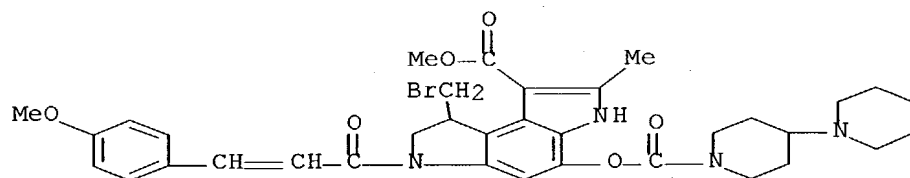
RN 146940-73-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



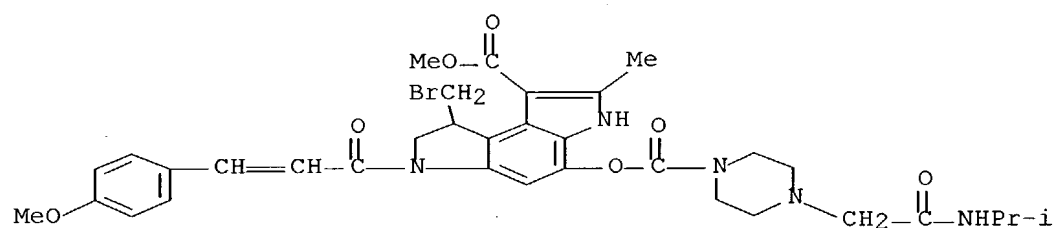
RN 146940-74-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-ylcarbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



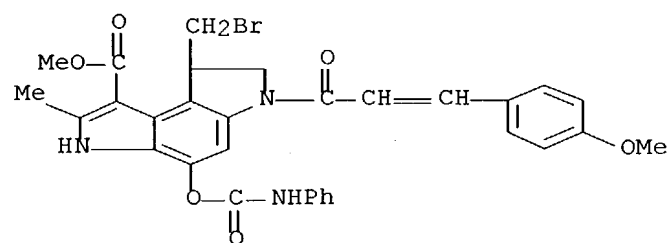
RN 146940-75-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-[2-[(1-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 146940-76-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[phenylamino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 97 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:160700 CAPLUS Full-text

DN 118:160700

TI Analysis of DNA fragmentation in human uterine cervix carcinoma HeLa S3 cells treated with duocarmycins or other antitumor agents by pulse field gel electrophoresis

AU Okamoto, Akihiko; Okabe, Masami; Gomi, Katsushige

CS Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Nagaizumi, 411, Japan

SO Japanese Journal of Cancer Research (1993), 84(1), 93-8

CODEN: JJCREP; ISSN: 0910-5050

DT Journal

LA English

AB Pulse field gel electrophoresis using a contour-clamped homogeneous elec. field was applied for the anal. of DNA-fragmenting activity of antitumor agents towards human uterine cervix carcinoma HeLa S3 cells. Duocarmycins (DUMs), novel antitumor antibiotics with ultrapotent cell growth-inhibitory activities, caused DNA fragmentation at 10 times their IC50 values at 2 h exposure. At 100 times their IC50 values, the size of the smallest fragments was about 245 kilobase pairs (kbp). DUMA, DUMB1 and DUMB2 exhibited similar DNA fragmentation patterns, suggesting similar action mechanisms. DNA fragmentation was also detected in cells treated with radical producers, intercalators and topoisomerase inhibitors. Two bands of about 1800 and 1500 kbp were commonly detected in the cells treated with DUMs and these agents. In addition, fragments of about 900 kbp were detected in the cells treated with a topoisomerase inhibitor, 4'-(9-acridinylamino)methanesulfon-m-anisidine, and fragments in the broad size range between 700 and 245 kbp in the cells treated with radical producers, bleomycin and neocarzinostatin. DUMs showed a characteristic DNA fragmentation pattern, since both types of fragments induced by the topoisomerase inhibitor and the radical producers were simultaneously detected, suggesting a novel mode of interaction with DNA. DNA-crosslinking agents and mitotic inhibitors did not induce DNA fragmentation under these conditions. The pulse field gel electrophoresis is potentially useful for characterizing DNA-cleaving activity of various antitumor agents at the cellular level.

L10 ANSWER 98 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:38908 CAPLUS Full-text

DN 118:38908

TI Preparation of DC-89 derivatives

IN Saito, Hiromitsu; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

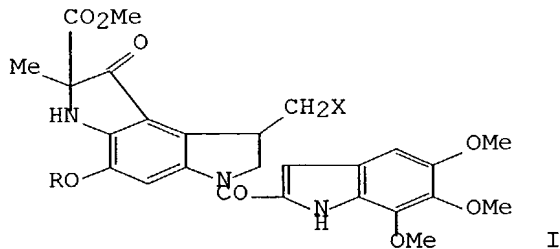
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	EP 499130	A1	19920819	EP 1992-101913	19920205
	R: DE, FR, GB, IT				
	JP 05051384	A2	19930302	JP 1992-20059	19920205
PRAI	JP 1991-21243		19910215		

OS MARPAT 118:38908
GI



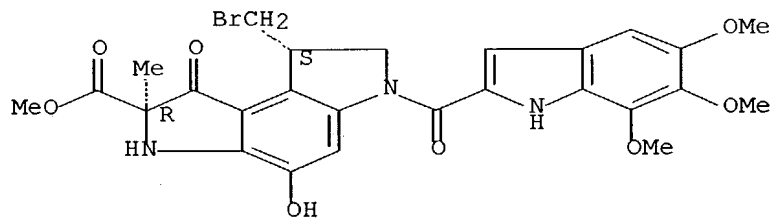
AB Title compds. I (X = Br, Cl; R = R1O2S, CO(CH2)nR2, wherein R1 = C1-6 alkyl, Ph, R2 = substituted heterocyclyl, n = 0-5) or a salt thereof, useful as antitumor agents, are prepared To DC-89B2 in CH2Cl2 was added DCC in CH2Cl2 followed by 3-(4-morpholinocarbonyl)propionic acid in CH2Cl2 to give I (X = Br, R = 4-morpholino-1-oxobutanoyl) (II). The IC50 of II on growth inhibitory effect against HeLaS3 cells was 0.054 nM.

IT **124325-94-6**, DC 89B2
RL: RCT (Reactant); RACT (Reactant or reagent)
(mesylation of)

RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

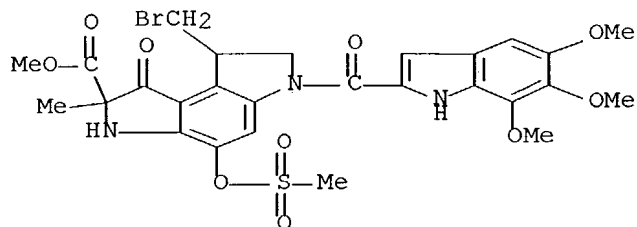


IT	144258-83-3P	144258-84-4P	144258-85-5P
	144258-86-6P	144258-87-7P	144258-88-8P
	144258-89-9P	144258-90-2P	144258-91-3P
	144258-92-4P	144258-93-5P	144258-94-6P
	144773-23-9P	144773-24-0P	144773-25-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as antitumor agent)

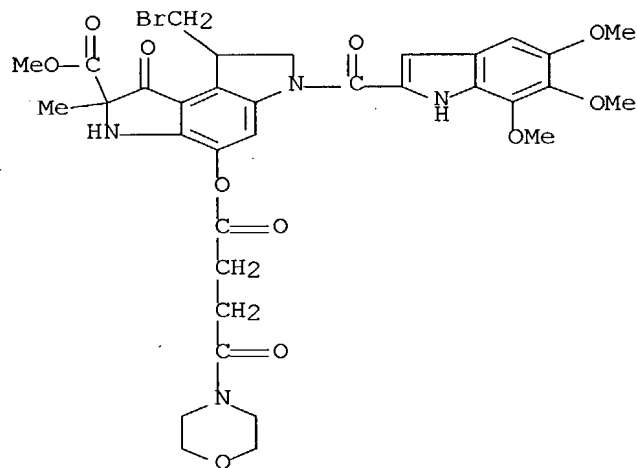
RN 144258-83-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



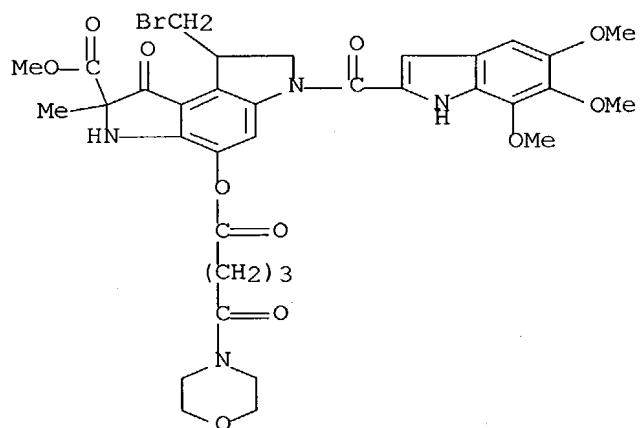
RN 144258-84-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1,4-dioxobutoxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA
INDEX NAME)



RN 144258-85-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1,5-
dioxopentyl]oxy]-
1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI)
(CA INDEX NAME)

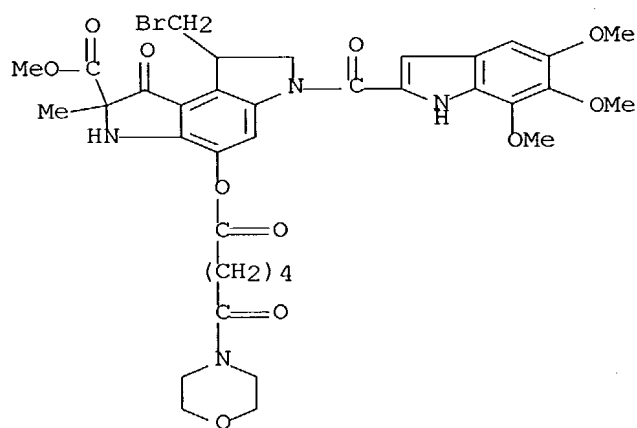


RN 144258-86-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[6-(4-morpholinyl)-1,6-
dioxohexyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI)

(CA

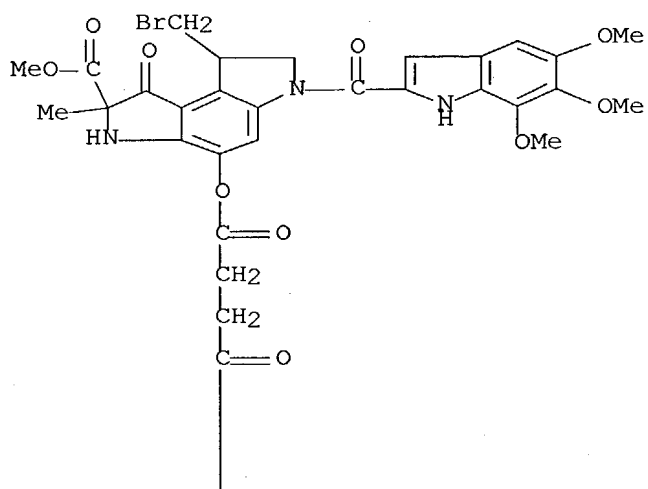
INDEX NAME)



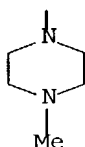
RN 144258-87-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-methyl-1-piperazinyl)-1,4-
dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl
ester (9CI) (CA INDEX NAME)

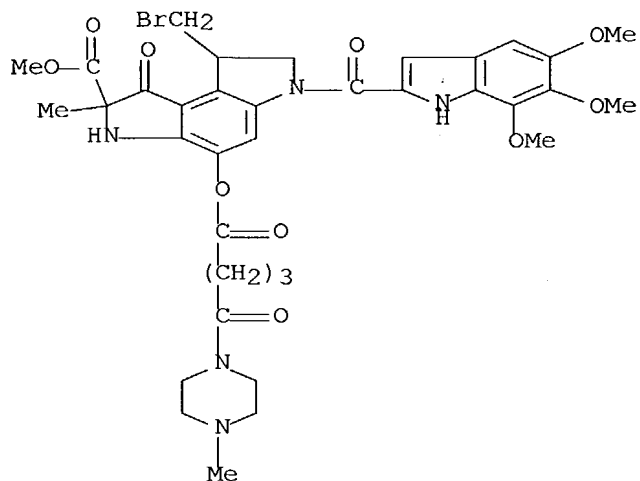
PAGE 1-A



PAGE 2-A



RN 144258-88-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-methyl-1-piperazinyl)-1,5-
 dioxopentyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-,
 methyl ester (9CI) (CA INDEX NAME)

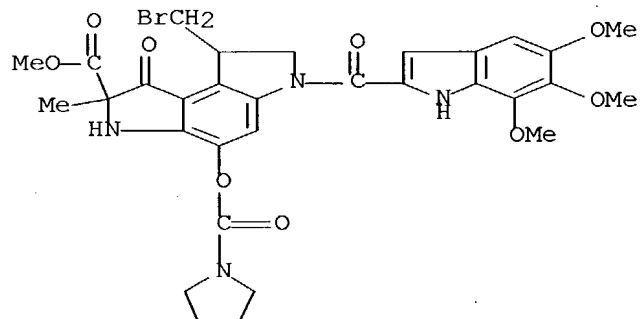


RN 144258-89-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-pyrrolidinylcarbonyl)oxy]-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA

INDEX

NAME)

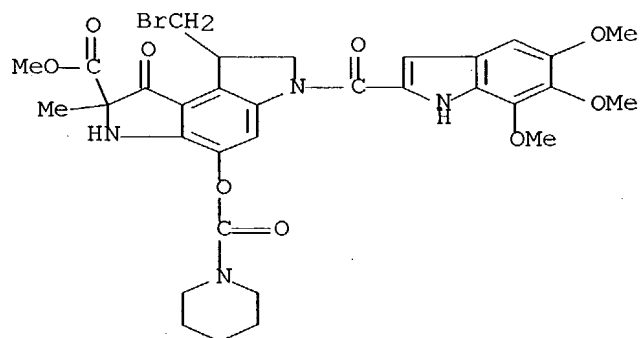


RN 144258-90-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-piperidinylcarbonyl)oxy]-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA

INDEX

NAME)

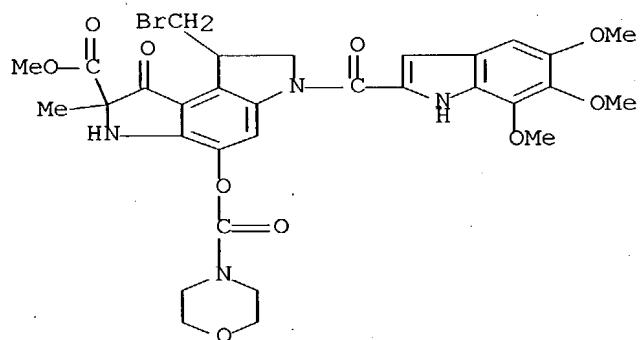


RN 144258-91-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-morpholinylcarbonyl)oxy]-1-oxo-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA

INDEX

NAME)

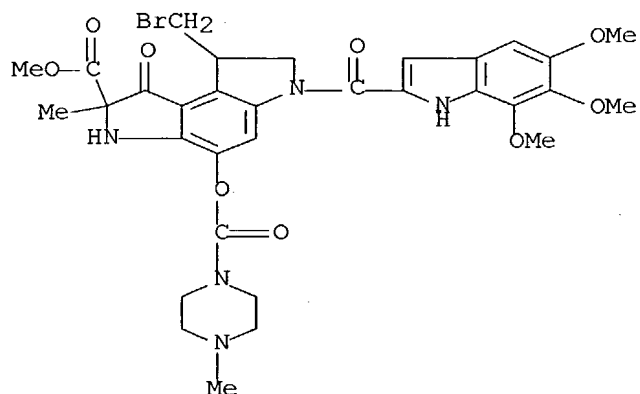


RN 144258-92-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[4-methyl-1-
piperazinyl)carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI)

(CA

INDEX NAME)

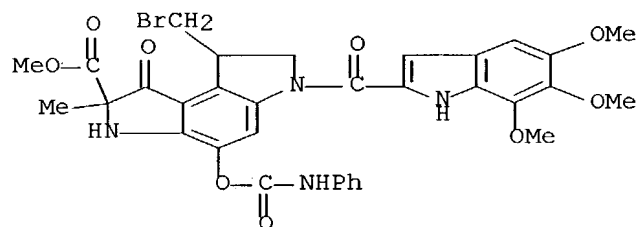


RN 144258-93-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[[(phenylamino) carbonyl]oxy]-6-
[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester (9CI) (CA

INDEX

NAME)

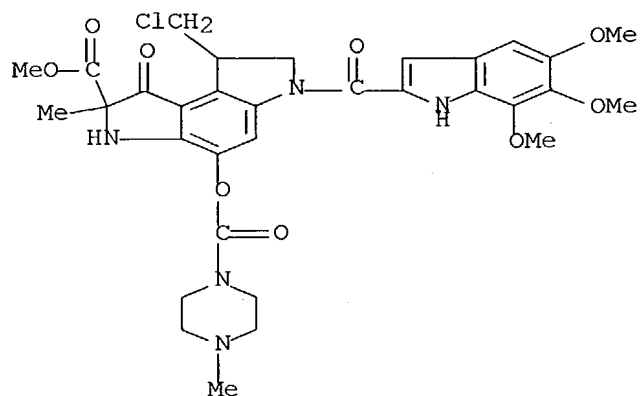


RN 144258-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-
piperazinyl) carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester (9CI)

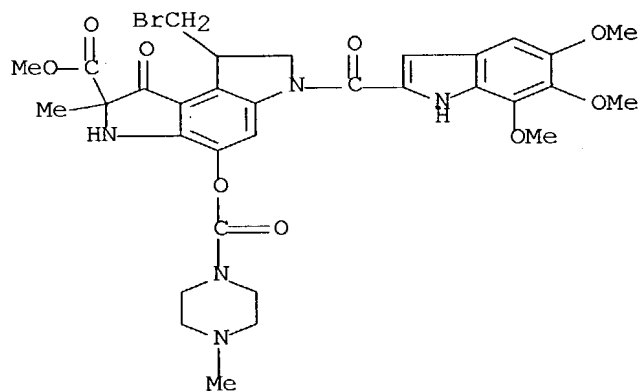
(CA

INDEX NAME)



RN 144773-23-9 CAPLUS

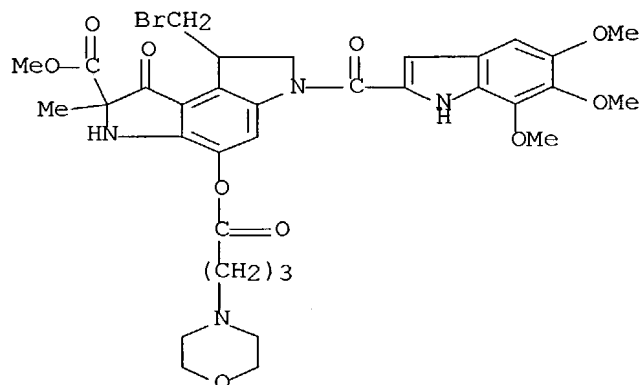
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 144773-24-0 CAPLUS

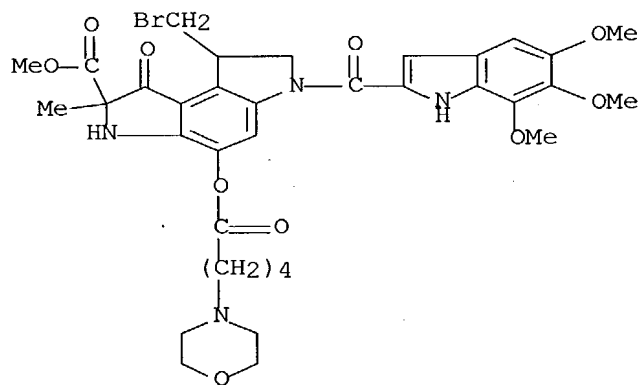
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1-oxobutoxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 144773-25-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1-oxopentyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



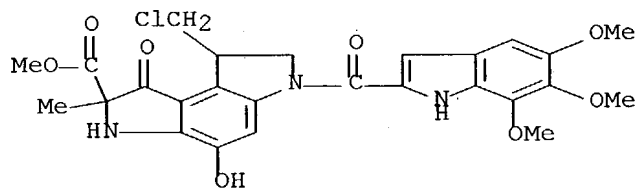
● HCl

IT 128517-09-9, DC 89A2

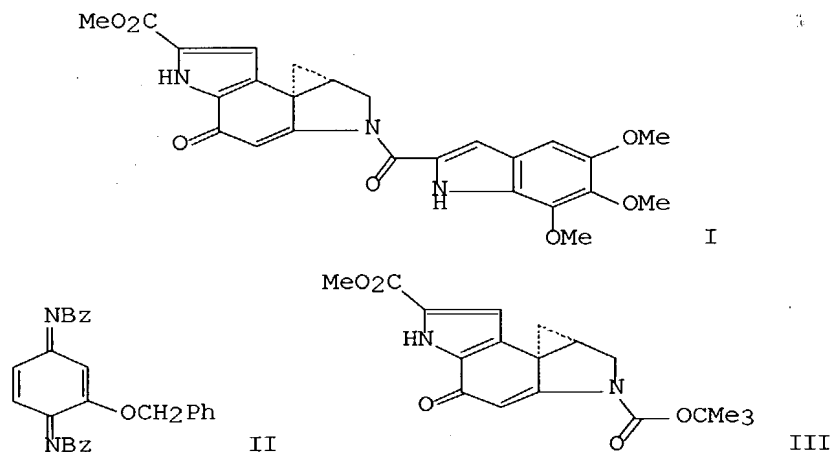
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of antitumor agents)

RN 128517-09-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 99 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:38646 CAPLUS Full-text
 DN 118:38646
 TI Total synthesis of (+)-duocarmycin SA
 AU Boger, Dale L.; Machiya, Kozo
 CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
 SO Journal of the American Chemical Society (1992), 114(25), 10056-8
 CODEN: JACSAT; ISSN: 0002-7863
 DT Journal
 LA English
 OS CASREACT 118:38646
 GI



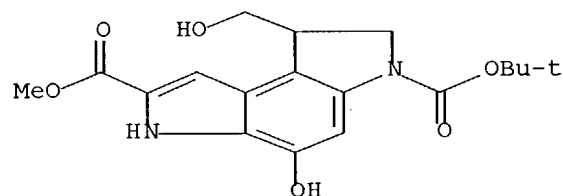
AB A concise total synthesis of natural (+)-duocarmycin SA (I) is based on sequential regioselective nucleophilic substitution reactions of the unsym. p-quinone diimide II leading to a dihydropyrroloindole precursor to the left-hand subunit. In addition to constituting a new synthetic strategy for the preparation of agents related to the natural or synthetic members of the duocarmycin class of antitumor-antibiotics, both enantiomers of N-BOC DSA (III) and its immediate synthetic precursors are now available. This provides access to synthetic analogs incorporating either enantiomer of the exceptionally stable and potent duocarmycin SA alkylation subunit.

IT **144667-36-7P 144732-55-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)(preparation and chlorination of)

RN 144667-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 7,8-dihydro-4-hydroxy-8-(hydroxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl
 ester (9CI) (CA INDEX NAME)

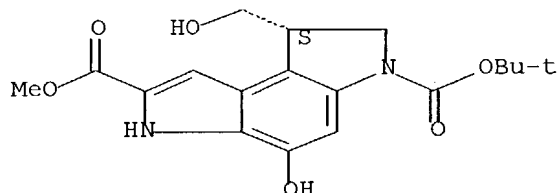


RN 144732-55-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid,

1,6-dihydro-5-hydroxy-1-(hydroxymethyl)-, 3-(1,1-dimethylethyl) 7-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



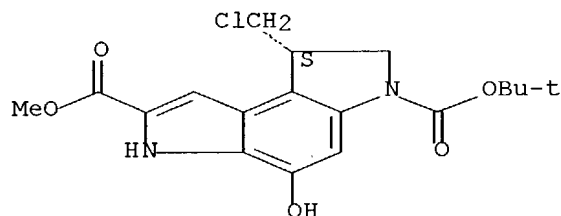
IT 144786-07-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, duocarmycin SA)

RN 144786-07-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

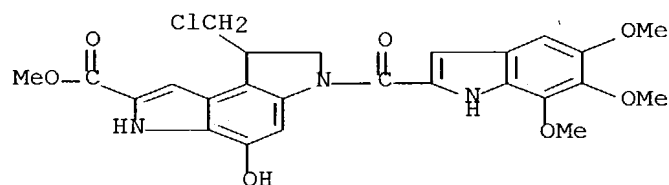


IT 144667-38-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent) (preparation and cyclopropanation of)

RN 144667-38-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-
yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

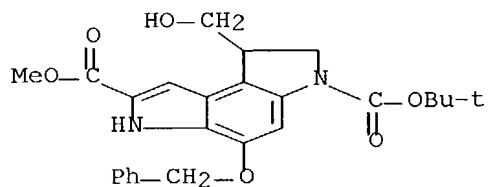


IT 144667-35-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent) (preparation and hydrogenolysis of)

RN 144667-35-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester (9CI) (CA INDEX NAME)

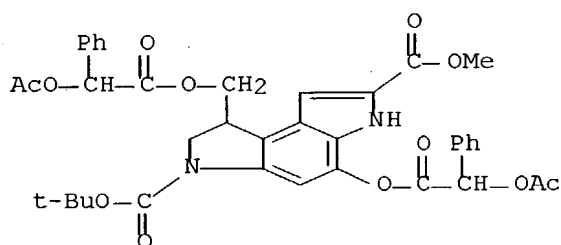


IT **144667-39-0P 144732-56-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent) (preparation and hydrolysis of)

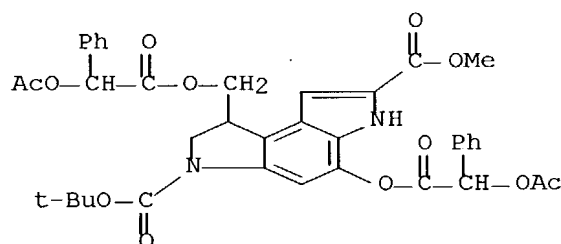
RN 144667-39-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 4-[[[(acetyloxy)phenylacetyl]oxy]-8-
 [[[acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-, 6-(1,1-
 dimethylethyl) 2-methyl ester, [8R-[4(R*),8R*(R*)]]-(9CI) (CA INDEX
 NAME)



RN 144732-56-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
 4-[[[(acetyloxy)phenylacetyl]oxy]-8-
 [[[acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-, 6-(1,1-
 dimethylethyl) 2-methyl ester, [8S-[4(S*),8R*(S*)]]-(9CI) (CA INDEX
 NAME)



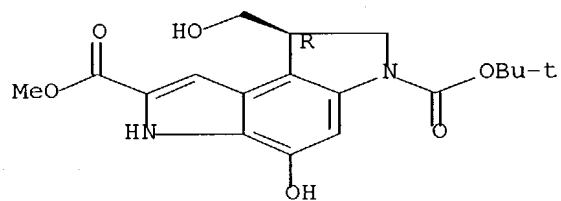
IT **144732-54-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 144732-54-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid,
 1,6-dihydro-5-hydroxy-1-(hydroxymethyl)-, 3-(1,1-dimethylethyl) 7-methyl
 ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

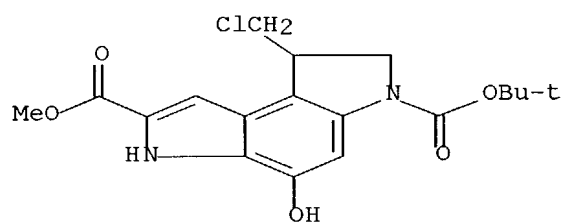


IT **144667-37-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, deblocking, and reaction of, with
trimethoxyindolecarboxylic acid)

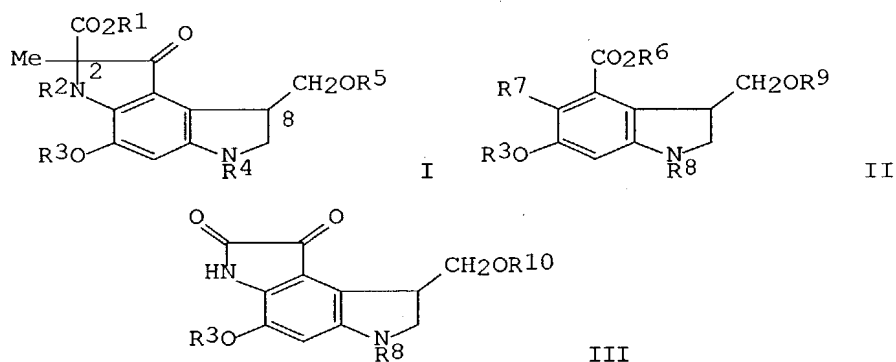
RN 144667-37-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-hydroxy-, 6-(1,1-dimethylethyl) 2-methyl
ester (9CI) (CA INDEX NAME)



L10 ANSWER 100 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1992:591827 CAPLUS Full-text
 DN 117:191827
 TI Preparation of 2-alkoxycarbonyl-2-methyl-1-oxo-1,2,3,6,7,8-hexahydrobenzo[1,2-b;4,3-b']dipyrrole derivatives as intermediates for duocarmycins
 IN Terajima, Atsuro; Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio
 PA Sagami Chemical Research Center, Japan
 SO Jpn. Kokai Tokkyo Koho, 27 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 04117383	A2	19920417	JP 1990-159828	19900620
	JP 3037965	B2	20000508		
PRAI	JP 1990-159828		19900620		
OS	MARPAT 117:191827				
GI					



AB The title compds. (I; R1 = H, C1-6 linear or branched alkyl; R2, R4 = H, amino-protecting group; R3, R5 = H, hydroxy-protecting group) and their intermediates [II and III; R3, R9, R10 = H, hydroxy-protecting group; R6 = H, C1-6 linear or branched alkyl; R7 = (un)substituted amino; R8 = H, amino-protecting group] are prepared I are useful as intermediates for the anticancer agents duocarmycin A, B1, C1 (pyrindamycin B), and C2 (pyrindamycin A). Thus, oxidation of III (R3 = PhCH2, R8 = CO2CMe3, R10 = SiMe2CMe3) (preparation given) with m-ClC6H4CO2OH in CH2Cl2 and methanolysis of the resulting isatoic acid anhydride derivative in the presence of K2CO3 gave II (R3 = PhCH2, R6 = Me, R7 = H2N, R8 = CO2CMe3, R9 = SiMe2CMe3). Alkylation of this with BrCHMeCO2Me in the presence of Cs2CO3 in DMF and formylation of the resultant II (R7 = NHCHMeCO2Me; R3, R6-R9 = same as above) gave II [R7 = N(CHO)CHMeCO2Me; R3, R6-R9 = same as above], which was cyclized by treatment with (Me2CH)2NLi in THF at -78° for 5.5 h to give (2R*,8S*)- and (2S*,8S*)-I (R1 = Me, R2 = CHO, R3 = PhCH2, R4 = CO2CMe3, R5 = SiMe2CMe3). These were converted into dl-duocarmycin A or -epiduocarmycin A.

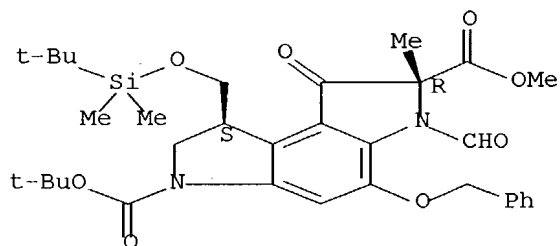
IT 132628-67-2P 132628-68-3P 132628-69-4P
 132628-70-7P 132628-71-8P 132628-72-9P
 143314-85-6P 143314-86-7P 143314-87-8P
 143314-88-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as intermediate for duocarmycins or pyrindamycins)

RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
 tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 2-methyl ester, trans- (9CI) (CA INDEX NAME)

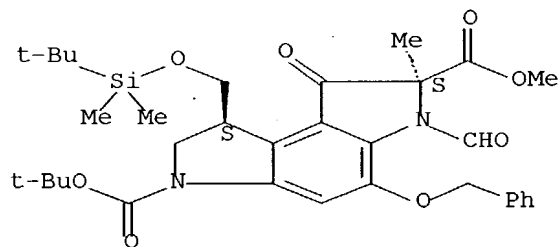
Relative stereochemistry.



RN 132628-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
 tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 2-methyl ester, cis- (9CI) (CA INDEX NAME)

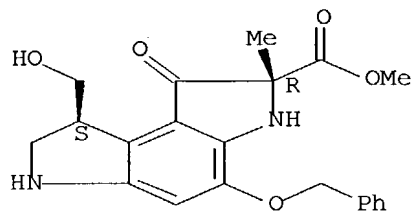
Relative stereochemistry.



RN 132628-69-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-
 (hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, methyl ester,
 dihydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

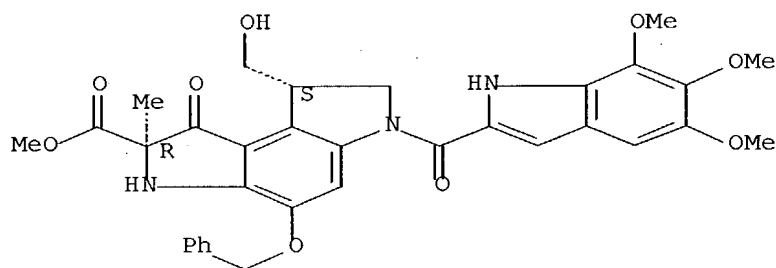


●2 HCl

RN 132628-70-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

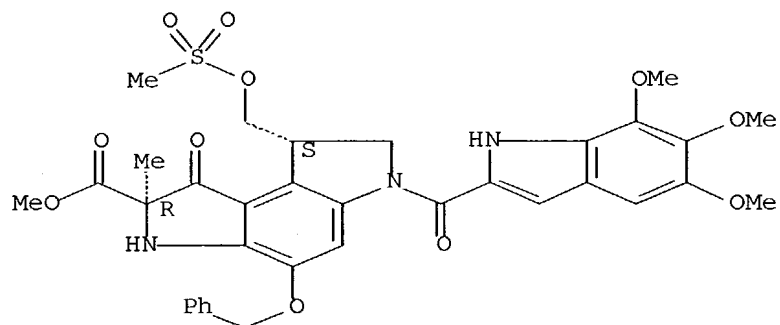
Relative stereochemistry.



RN 132628-71-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



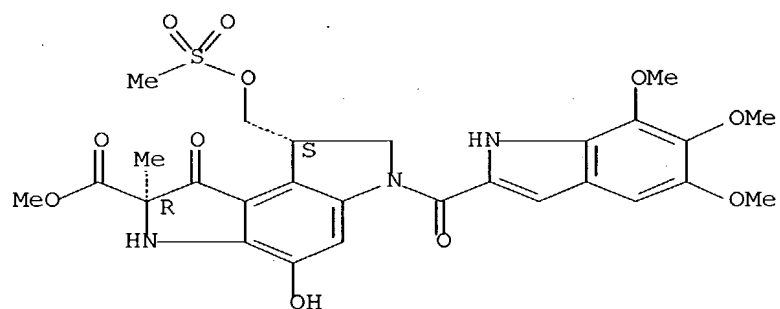
RN 132628-72-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA

INDEX

NAME)

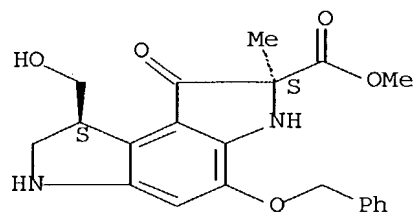
Relative stereochemistry.



RN 143314-85-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, methyl ester, dihydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

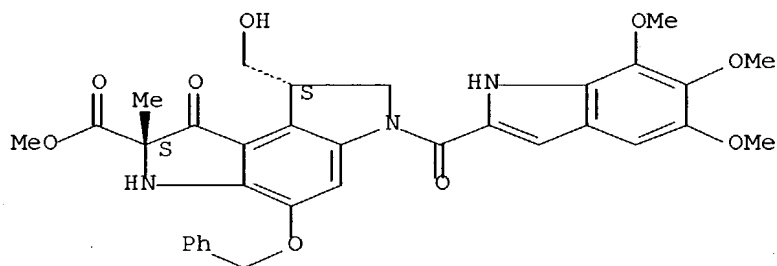


●2 HCl

RN 143314-86-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

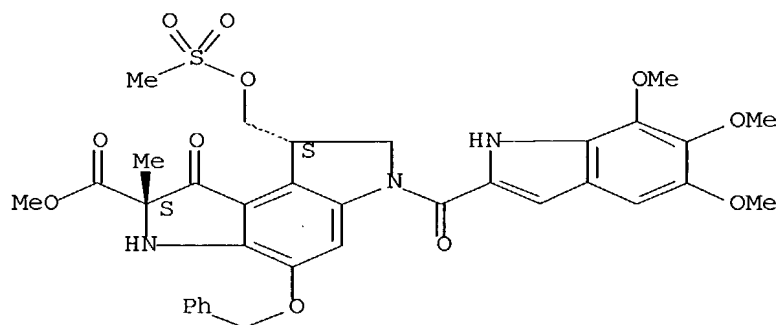
Relative stereochemistry.



RN 143314-87-8 CAPLUS

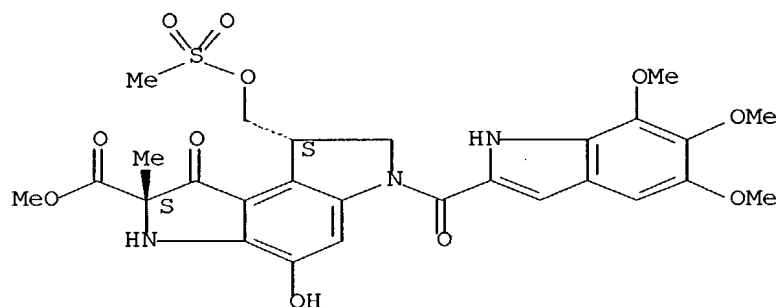
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



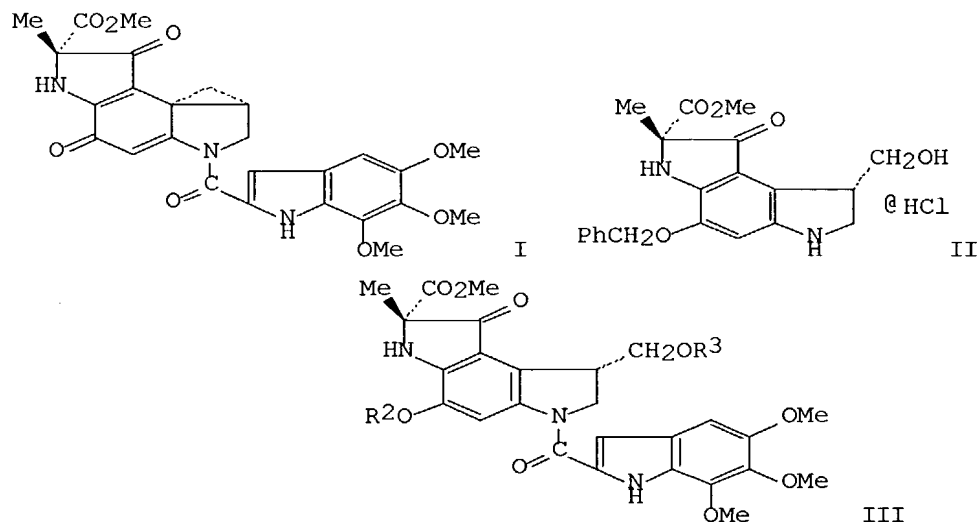
RN 143314-88-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L10 ANSWER 101 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1992:591589 CAPLUS Full-text
 DN 117:191589
 TI Preparation of 2-epiduocarmycin A as antitumor agent
 IN Terajima, Atsuro; Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio
 PA Zaidan Hojin Sagami Chuo Kagaku Kenkyusho, Japan
 SO Jpn. Kokai Tokkyo Koho, 24 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	JP 04099774	A2	19920331	JP 1990-213741	19900814
PRAI	JP 1990-213741		19900814		
OS	MARPAT 117:191589				
GI					



AB 2-Epiduocarmycin A (I) and its intermediates are prepared Condensation of (2S,8S)-II with 6,7,8-trimethoxy-1H-indole-2-carboxylic acid and 1-(3-dimethylaminopropyl)ethylcarbodiimide HCl in DMF gave 62% indolyl derivative (2S,8S)-III (R2 = PhCH2, R3 = H), which was mesylated with MeSO2Cl in CH2Cl2 to give 99% mesylate (2S,8S)-III (R2 = PhCH2, R3 = MeSO2) (IV). Hydrogenolysis of IV over 10% Pd-C gave 83% phenolic derivative (2S,8S)-III (R2 = H, R3 = MeSO2), which was treated with NaH (50% oil dispersion) in THF with stirring at room temperature to give 56% (DL)-I, which showed IC50 of 1.7 ± 10^{-4} $\mu\text{g/mL}$ against P-388 leukemic cells.

IT 132628-67-2P 132628-68-3P 132628-69-4P
 132628-70-7P 132628-71-8P 132628-72-9P
 143314-85-6P 143314-86-7P 143314-87-8P
 143314-88-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

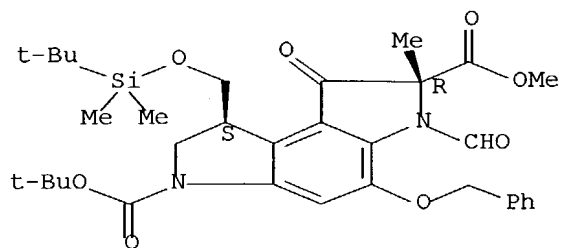
(Reactant or reagent)

(preparation and reaction of, in preparation of antitumor agent)

RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
 tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
 2-methyl ester, trans- (9CI) (CA INDEX NAME)

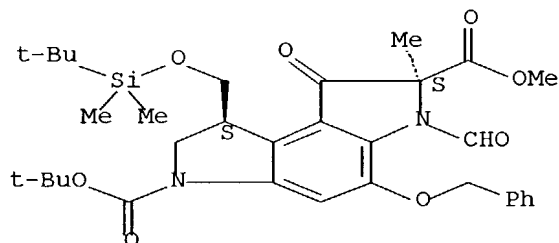
Relative stereochemistry.



RN 132628-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, cis- (9CI) (CA INDEX NAME)

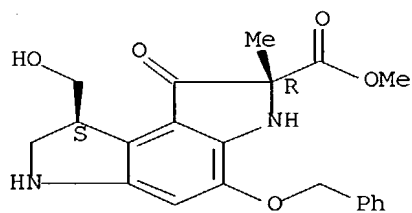
Relative stereochemistry.



RN 132628-69-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, methyl ester,
dihydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



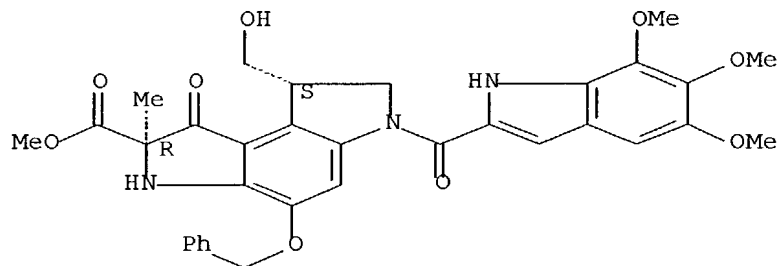
●2 HCl

RN 132628-70-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

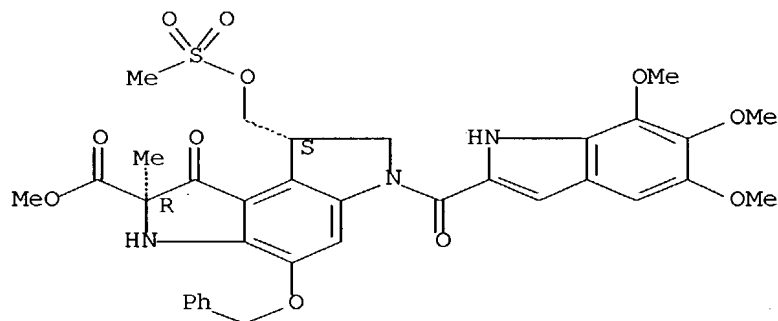
Relative stereochemistry.



RN 132628-71-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

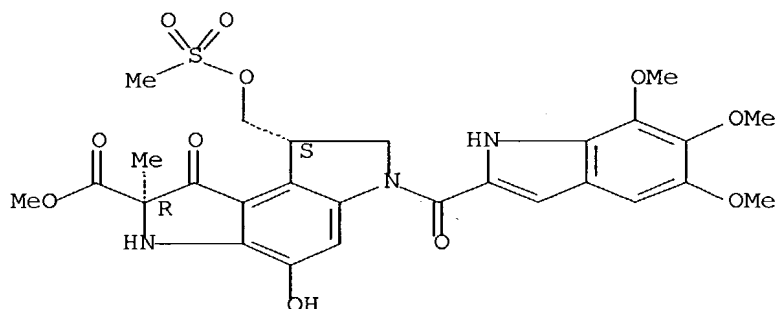
Relative stereochemistry.



RN 132628-72-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

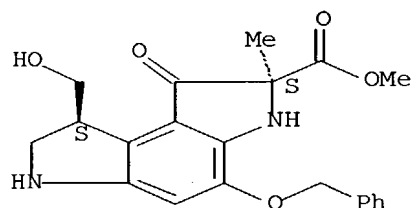
Relative stereochemistry.



RN 143314-85-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, methyl ester, dihydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

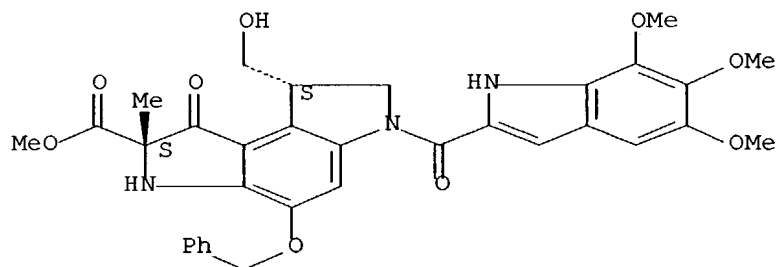


●2 HCl

RN 143314-86-7 CAPLUS

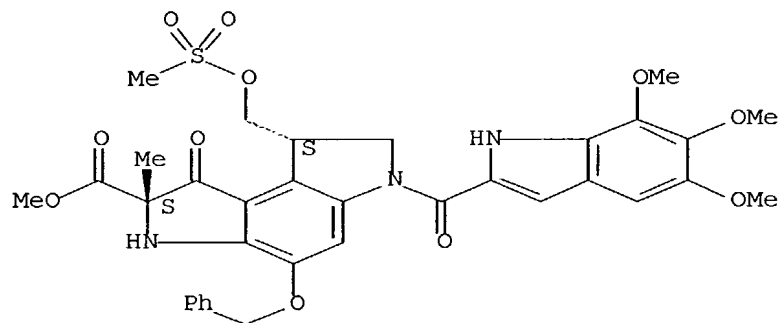
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



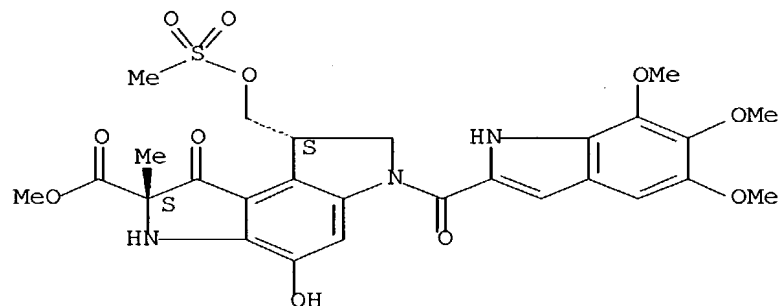
RN 143314-87-8 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 143314-88-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L10 ANSWER 102 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1992:143298 CAPLUS Full-text
 DN 116:143298
 TI Anticellular and antitumor activity of duocarmycins, novel antitumor antibiotics
 AU Gomi, Katsushige; Kobayashi, Eiji; Miyoshi, Katsunori; Ashizawa, Tadashi;

Okamoto, Akihiko; Ogawa, Tatsuhiro; Katsumata, Shigeo; Mihara, Akira; Okabe, Masami; Hirata, Tadashi

CS Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Nagaizumi, 411, Japan

SO Japanese Journal of Cancer Research (1992), 83(1), 113-20

CODEN: JJCREP; ISSN: 0910-5050

DT Journal

LA English

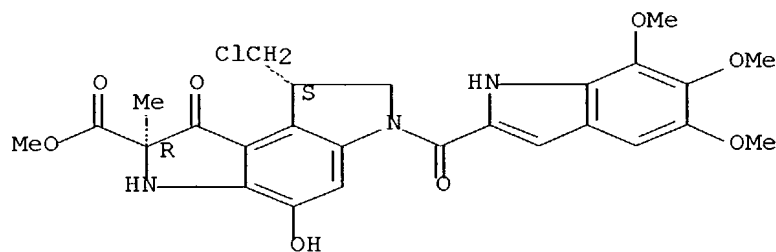
AB The anticellular and antitumor activities of duocarmycins (DUMs) were examined against human and murine tumor cells. DUMs consist of 5 compds., A, B1, B2, and C1, and C2, which possess a pharmacophore similar to that of CC-1065, a previously isolated antibiotic. DUMA exhibited ultrapotent growth-inhibitory activity with an IC50 value of 6 pM against human uterine cervix carcinoma HeLa S3 cells. DUMA and DUMB1 also inhibited the growth of adriamycin (ADM)-resistant lines of human nasopharynx carcinoma KB cells and breast carcinoma MCF-7 cells as well as their sensitive lines. DUMs inhibited the growth of s.c.-inoculated murine tumors such as B16 melanoma, sarcoma 180, M5076 sarcoma, and colon 26. DUMs were also effective in increasing the life span of i.p.-inoculated B16 melanoma-bearing mice, although their effect was marginal against other i.p. inoculated tumors. DUMB1 exhibited an activity superior to the other 4 compds. DUMB1 rapidly inhibited the incorporation of [3H]thymidine into macromols. of HeLa S3 cells as compared with that of [3H]uridine or [3H]leucine. DNA strand breaks were detected in DUMB1-treated HeLa S3 cells by agarose gel electrophoresis with a contour-clamped homogeneous elec. field apparatus. DUMs possess interesting biol. activities as DNA-targeting antitumor antibiotics.

IT **118292-36-7**, Duocarmycin C2 **124325-94-6**, Duocarmycin B2
 RL: PRP (Properties)
 (antitumor effects of, structure in relation to)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

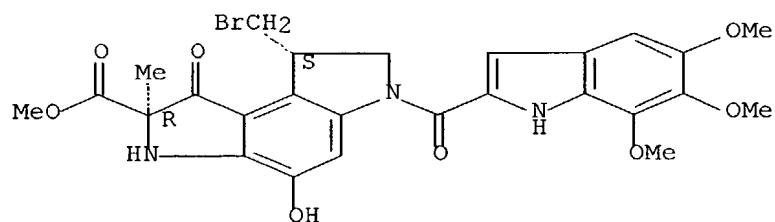
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

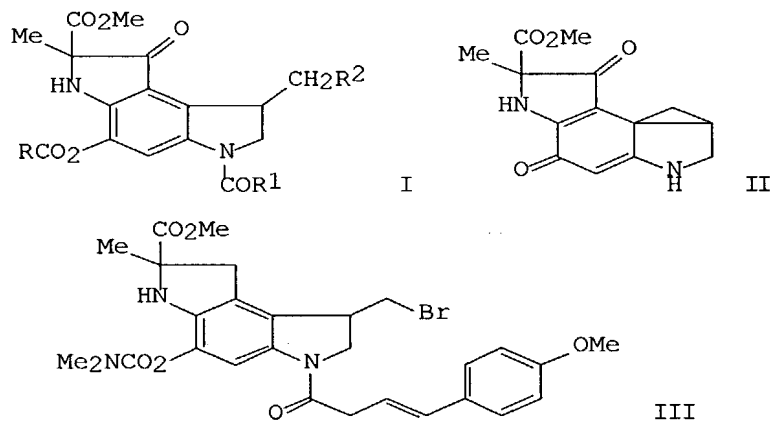
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 103 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1992:106269 CAPLUS Full-text
 DN 116:106269
 TI Preparation of DC-89 derivatives as neoplasm inhibitors
 IN Saito, Hiromitsu; Asai, Akira; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 25 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 461603	A1	19911218	EP 1991-109533	19910611
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5214065	A	19930525	US 1991-710407	19910605
	JP 04226988	A2	19920817	JP 1991-137741	19910610
	US 5248692	A	19930928	US 1993-24472	19930301
PRAI	JP 1990-152098		19900611		
	US 1991-710407		19910605		
OS	MARPAT 116:106269				
GI					



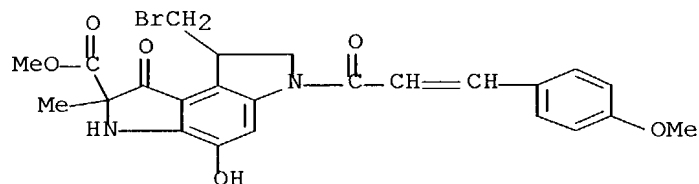
AB Title compds. [I; R = amino, morpholino, pyrrolidinyl, piperidinyl, homopiperidinyl, etc.; R1 = (substituted) phenylethenyl, phenoxyethyl, acylaminoindolyl; etc.; R2 = Cl, Br], were prepared. Thus, antibiotic DC-88A was stirred with NaOMe in MeOH to give 97% intermediate II. II was acylated with p-nitrophenyl 4-methoxycinnamate/NaH and the product was treated with aqueous HBr and then Me2NCOCl to give title compound III. III at 16 mg/kg i.v. in mice reduced the size of sarcoma 180 tumors to 7.8% of controls.

IT **128438-47-1P 128438-48-2P 128438-53-9P**
128438-56-2P 139147-60-7P 139147-61-8P
139147-62-9P 139147-63-0P 139147-64-1P
139147-65-2P 139147-66-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as intermediate for neoplasm inhibitor)

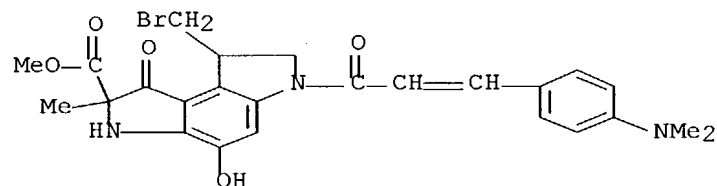
RN 128438-47-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



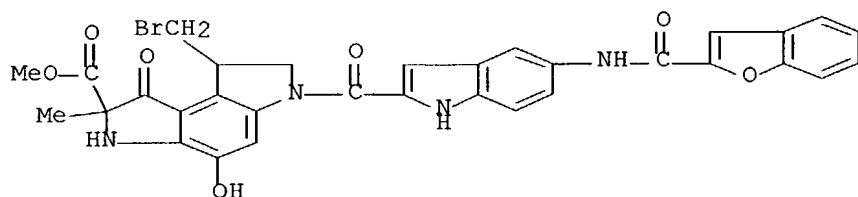
RN 128438-48-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



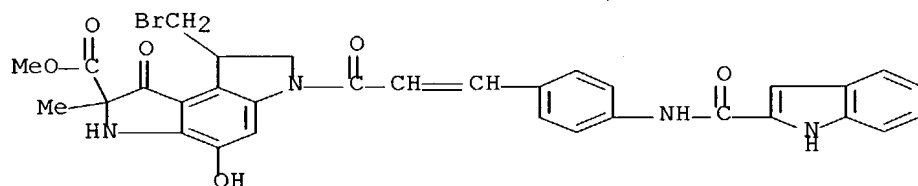
RN 128438-53-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



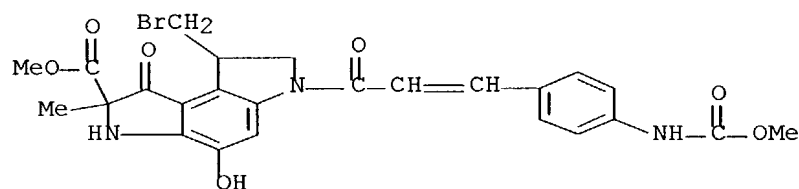
RN 128438-56-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-[4-[(1H-indol-2-ylcarbonyl)amino]phenyl]-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



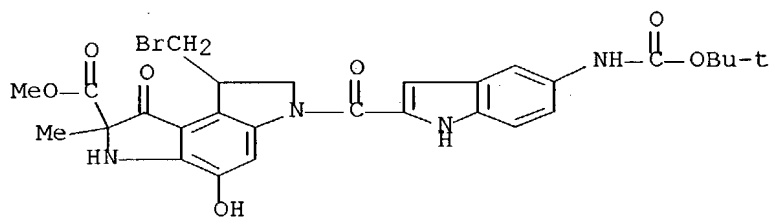
RN 139147-60-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-[4-[(methoxycarbonyl)amino]phenyl]-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



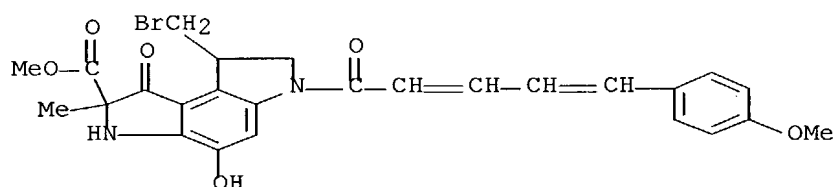
RN 139147-61-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[[5-[[[(1,1-dimethylethoxy)carbonyl]amino]-1H-indol-2-yl]carbonyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



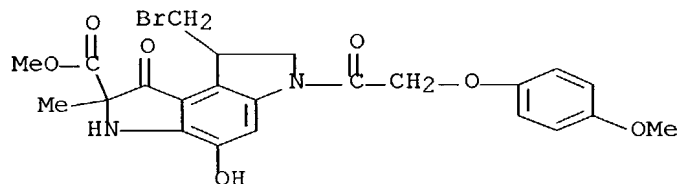
RN 139147-62-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[5-(4-methoxyphenyl)-1-oxo-2,4-pentadienyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



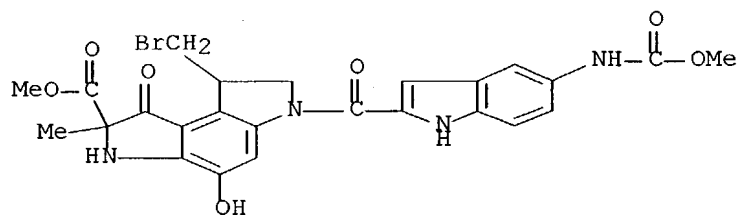
RN 139147-63-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[(4-methoxyphenoxy)acetyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



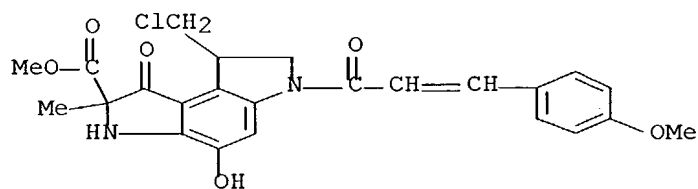
RN 139147-64-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[[5-[(methoxycarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



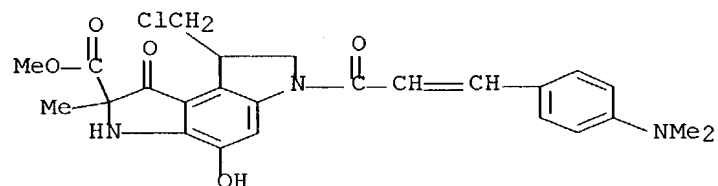
RN 139147-65-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-66-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-6-[3-(dimethylamino)phenyl]-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



IT 139147-43-6P 139147-44-7P 139147-45-8P
139147-46-9P 139147-47-0P 139147-48-1P
139147-49-2P 139147-50-5P 139147-51-6P
139147-52-7P 139147-53-8P 139147-54-9P
139147-55-0P 139147-56-1P 139147-57-2P
139147-58-3P 139147-59-4P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

use);

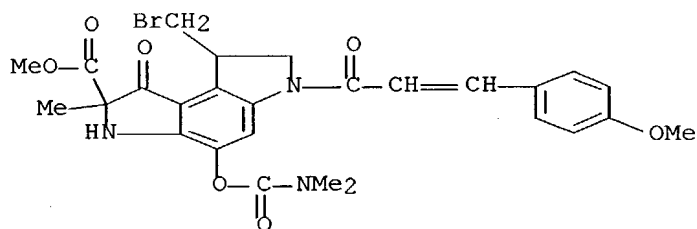
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor)

RN 139147-43-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-
methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI)

(CA

INDEX NAME)

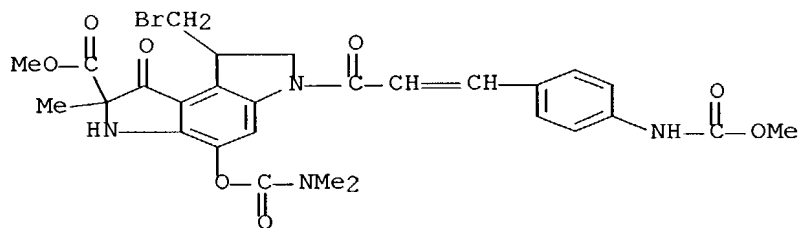


RN 139147-44-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-[4-
[(methoxycarbonyl) amino]phenyl]-1-oxo-2-propenyl]-2-methyl-1-oxo-,

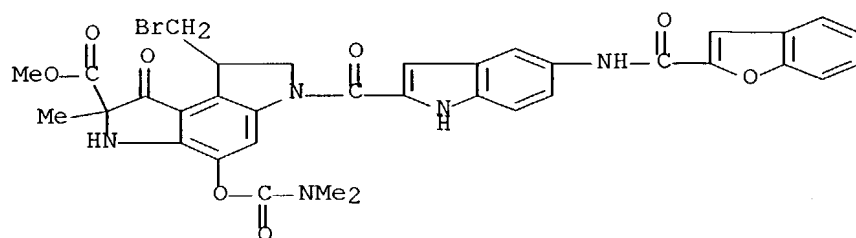
methyl

ester (9CI) (CA INDEX NAME)



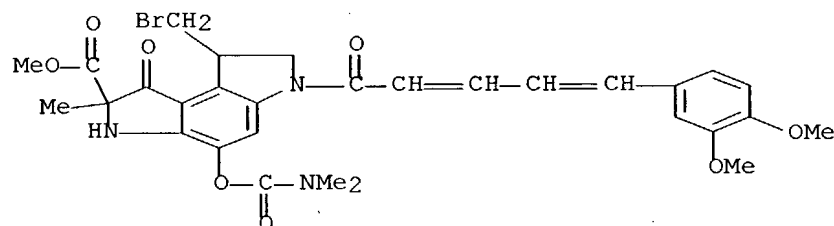
RN 139147-45-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[5-[(2-
benzofuranylcarbonyl) amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-,
methyl ester (9CI) (CA INDEX NAME)



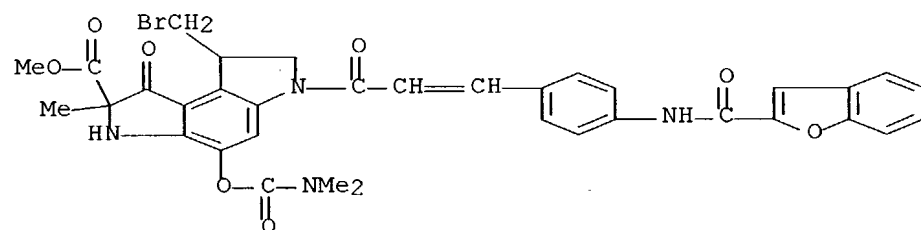
RN 139147-46-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[5-(3,4-dimethoxyphenyl)-1-oxo-2,4-pentadienyl]-4-[[dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-47-0 CAPLUS

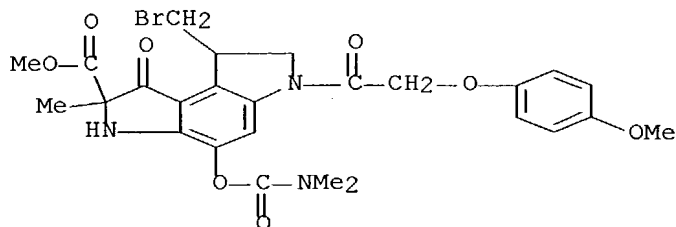
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-[4-[(2-benzofuranylcarbonyl)amino]phenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-4-[[dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-48-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[4-(2-benzofuranylcarbonyl)aminophenyl]-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

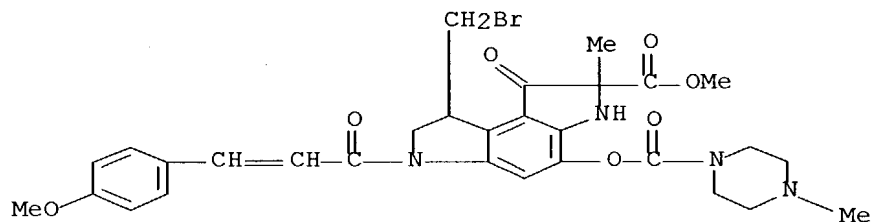
methoxyphenoxy)acetyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-49-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-

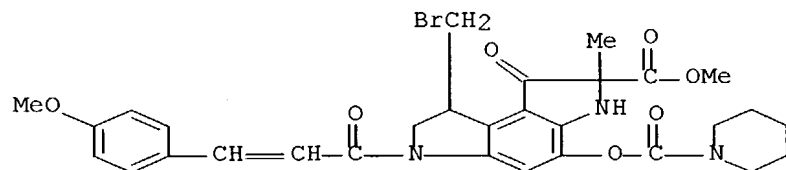
4-
[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-50-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-

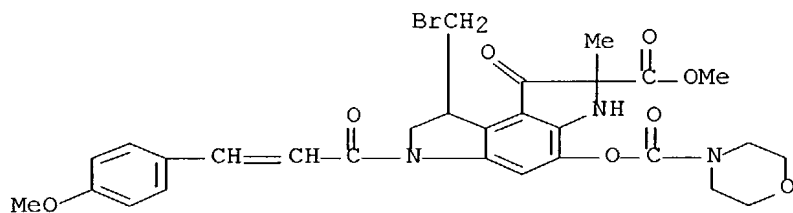
1-
oxo-4-[(1-piperidinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-51-6 CAPLUS

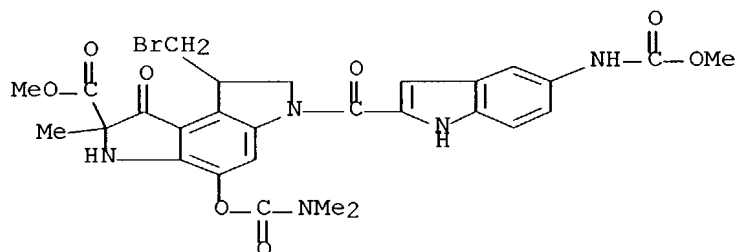
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-
4-
[(4-morpholinylcarbonyl)oxy]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



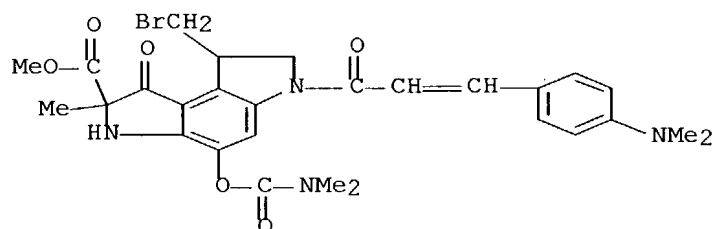
RN 139147-52-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[[5-
[(methoxycarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl
ester (9CI) (CA INDEX NAME)

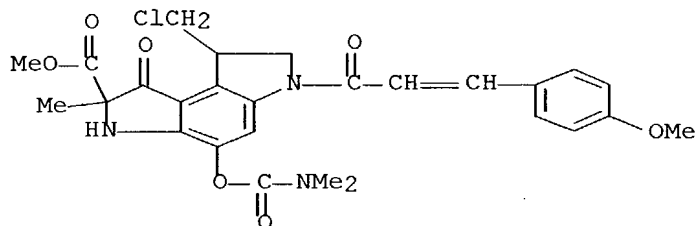


RN 139147-53-8 CAPLUS

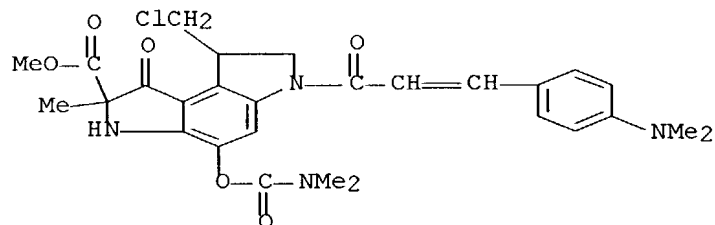
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-
propenyl]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA
INDEX NAME)



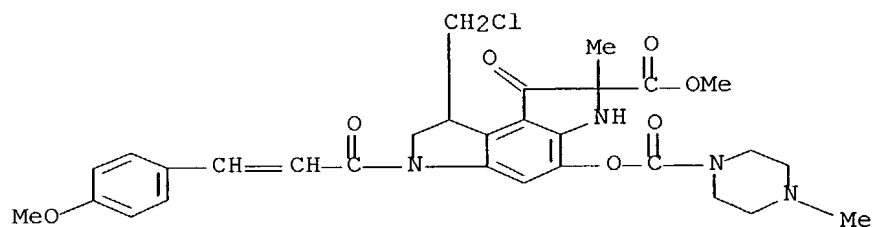
RN 139147-54-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-
 [[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-
 methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI)
 (CA INDEX NAME)



RN 139147-55-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-
 [[(dimethylamino) carbonyl]oxy]-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-
 propenyl]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA
 INDEX NAME)

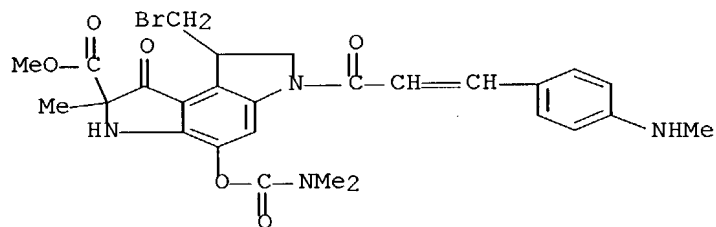


RN 139147-56-1 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-
 4-
 [[(4-methyl-1-piperazinyl) carbonyl]oxy]-1-oxo-, methyl ester (9CI) (CA
 INDEX NAME)



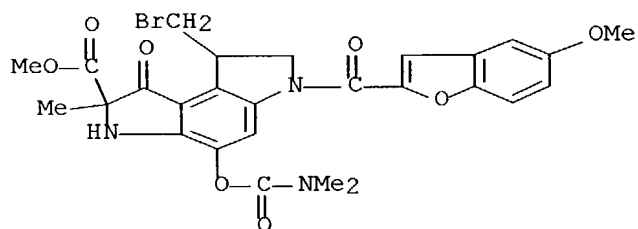
RN 139147-57-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[3-[4-(methylamino)phenyl]-1-oxo-2-propenyl]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-58-3 CAPLUS

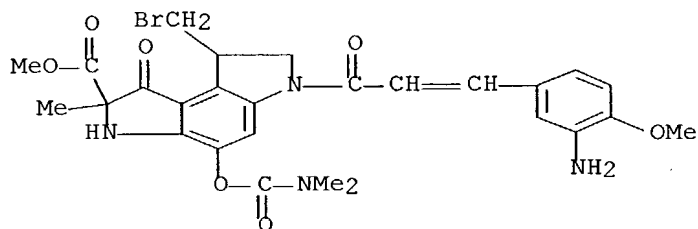
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(5-methoxy-2-benzofuranyl) carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-59-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-4-[[(dimethylamino) carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo- (9CI)

(CA INDEX NAME)



L10 ANSWER 104 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:99301 CAPLUS Full-text

DN 116:99301

TI Maleic anhydride copolymers as antidotes for the cytotoxicity of neoplasm

inhibitors

IN Bach, Ardalan; Shanahan, William R., Jr.

PA G.D. Searle and Co., USA

SO Eur. Pat. Appl., 27 pp.

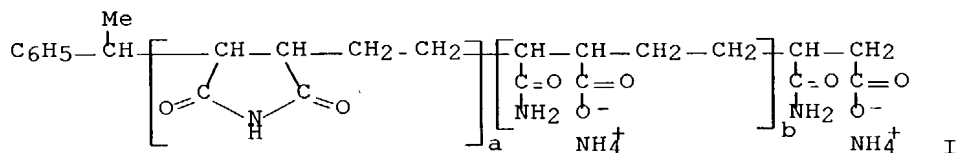
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 393575	A1	19901024	EP 1990-107246	19900417
	EP 393575	B1	19940316		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2014732	AA	19901017	CA 1990-2014732	19900417
	JP 02292227	A2	19901203	JP 1990-101530	19900417
	AT 102838	E	19940415	AT 1990-107246	19900417
	ES 2062155	T3	19941216	ES 1990-107246	19900417
PRAI	US 1989-339503		19890417		
	EP 1990-107246		19900417		
OS	MARPAT 116:99301				
GI					



AB Half-amide:half-imide copolymers comprising ethylene and maleic anhydride moieties (structure given), specifically carbetimer (I; a/b =

1:2-5), decrease the cytotoxic side effects of neoplasm inhibitors. Mice treated i.v. with 21 mg adriamycin/kg died within 5 days. When 1700 mg I/kg was administered concomitantly, no lethality was shown for >30 days.

IT **118292-36-7**, Pyrindamycin

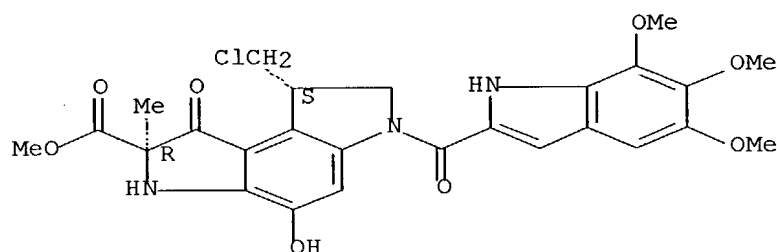
RL: PRP (Properties)

(cytotoxicity of, maleic anhydride copolymer antidote for)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 105 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:19720 CAPLUS Full-text

DN 116:19720

TI Antibiotics SF2582 manufacture with Streptomyces

IN Ohba, Kazunori; Watabe, Hiroomi; Nagasawa, Mieko; Sakakibara, Shiro; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi; Koyama, Masao; Nakazawa, Tadashi; Yamamoto, Haruo

PA Meiji Seika Kaisha, Ltd., Japan

SO U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 276,714, abandoned.

CODEN: USXXAM

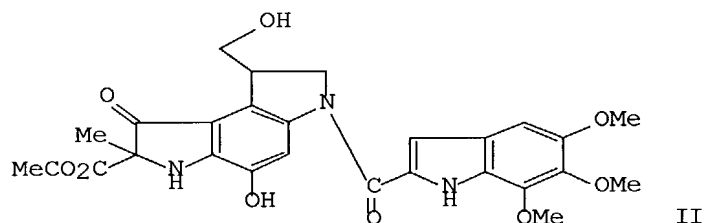
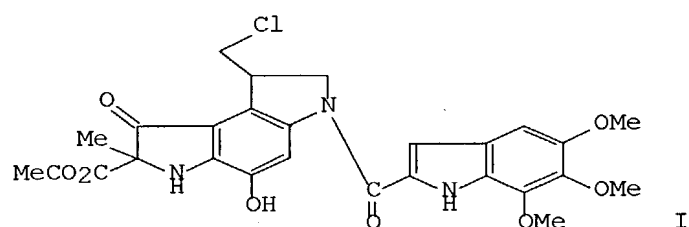
DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4994578	A	19910219	US 1989-344738	19890428
	JP 01139590	A2	19890601	JP 1987-297476	19871127
	JP 01265890	A2	19891023	JP 1988-94544	19880419
	JP 01275581	A2	19891106	JP 1988-103782	19880428
	JP 2562935	B2	19961211		
	US 5037993	A	19910806	US 1990-520424	19900508
PRAI	JP 1987-297476		19871127		
	JP 1988-94544		19880419		
	JP 1988-103782		19880428		
	US 1988-276714		19881128		
	US 1989-344738		19890428		

GI



AB The antibiotics SF2582 A (I), B, and C (II), also useful as neoplasm inhibitors, are manufactured by culture of Streptomyces. Derivs. of the antibiotics having improved antitumor activities are prepared Streptomyces SF2582 was shake-cultured for 5 days at 28°, and the cell mass from 1000 L culture broth recovered by filtration. I, antibiotic SF2582B, and II 182, 88, and 450 mg, resp., were recovered from the cell mass by extraction and chromatog. The sulfate or alkyl- or arylsulfonate derivs. (4) were prepared from II and their antitumor activity determined Against P388 cells, the derivs. had LC50 (ng/mL) of 4-2500, as compared to 9400 for II. Also given was the morphol. and physiol. characteristics of Streptomyces SF2582. The physicochem. characteristics of I, SF2582B, and II were also given.

IT **118292-36-7P**, Antibiotic SF 2582A **125600-37-5P**, Antibiotic SF 2582C

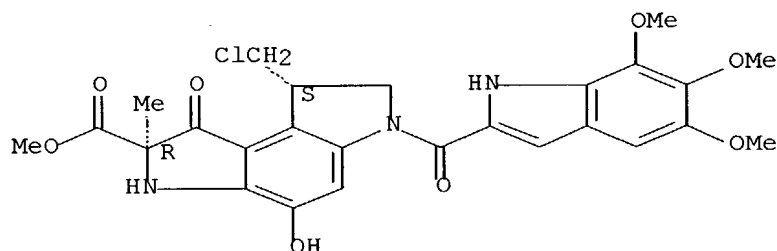
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

(manufacture of, with Streptomyces, as neoplasm inhibitor)

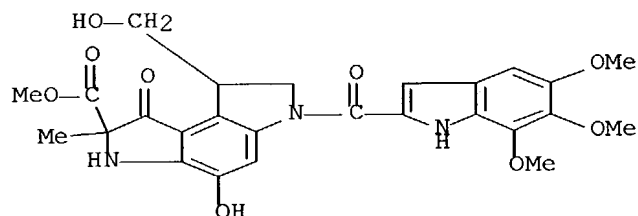
RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

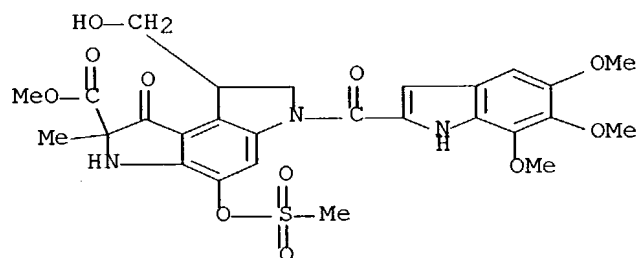


RN 125600-37-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-8-(hydroxymethyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

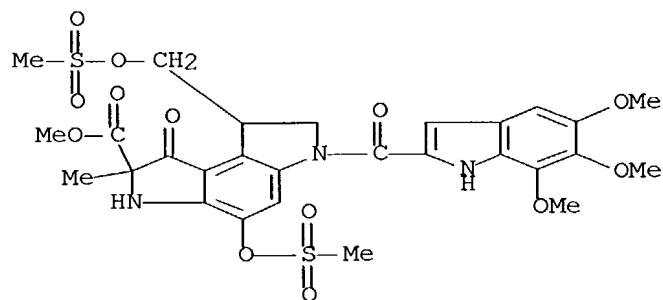


IT 126590-90-7P 136483-61-9P 136483-62-0P
 136772-69-5P
 RL: PREP (Preparation)
 (preparation of, from antibiotic SF2582C, enhanced antitumor activity of)

RN 126590-90-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

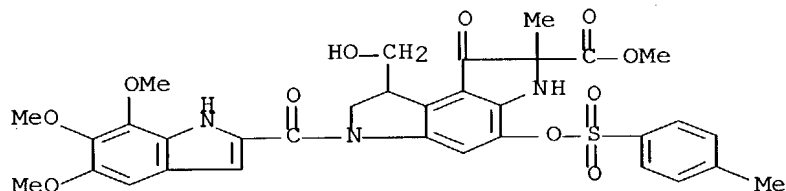


RN 136483-61-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-4-[(methylsulfonyl)oxy]-8-[[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



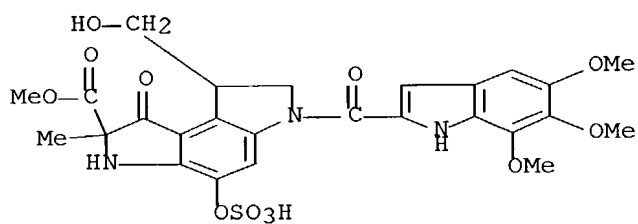
RN 136483-62-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-4-[[(4-methylphenyl) sulfonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 136772-69-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(sulfooxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 106 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1991:654225 CAPLUS Full-text

DN 115:254225

TI Duocarmycins, new antitumor antibiotics produced by Streptomyces;

producing organisms and improved production

AU Ichimura, Michio; Ogawa, Tatsuhiko; Katsumata, Shigeo; Takahashi, Keiichi; Takahashi, Isami; Nakano, Hirofumi

CS Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan

SO Journal of Antibiotics (1991), 44(10), 1045-53

CODEN: JANTAJ; ISSN: 0021-8820

DT Journal

LA English

AB Improved culture conditions were designed to produce high titer of duocarmycins B1, B2, C1, and C2, halogenated seco-compds. of duocarmycin A. Duocarmycin SA, one of the most potent cytotoxic agents yet discovered is more stable in culture media than duocarmycin A, despite the structural similarity on their spirocyclopropylhexadienone moiety. In contrast to the duocarmycin A fermentation, no halogenated seco-compds. of duocarmycin SA were detected in culture broth supplemented with Br⁻ and Cl⁻. All duocarmycins could be produced using one producing strain with improved media and culture conditions.

IT **118292-36-7P**, Duocarmycin C2 **124325-94-6P**, Duocarmycin B2

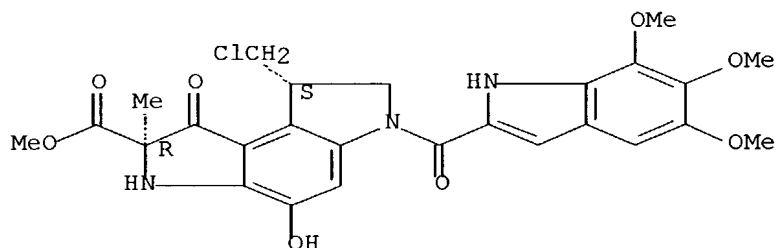
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

(manufacture of, with Streptomyces)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

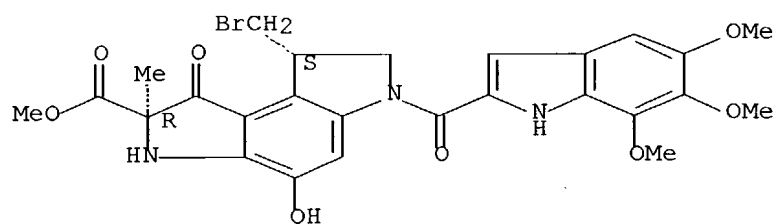
Absolute stereochemistry.



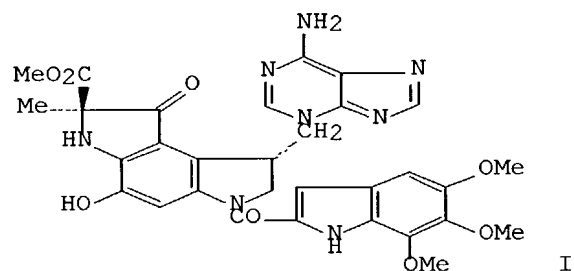
RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

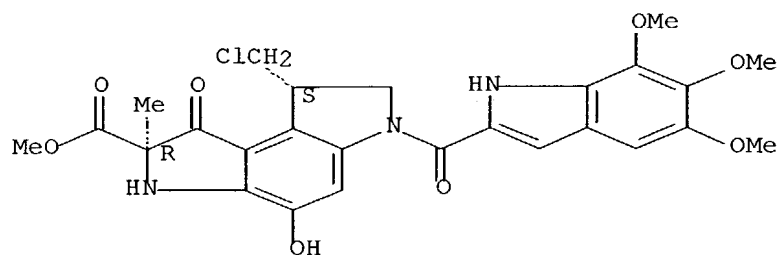


L10 ANSWER 107 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:484929 CAPLUS Full-text
 DN 115:84929
 TI Isolation and characterization of the duocarmycin-adenine DNA adduct
 AU Boger, Dale L.; Ishizaki, Takayoshi; Zarrinmayeh, Hamideh
 CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
 SO Journal of the American Chemical Society (1991), 113(17), 6645-9
 CODEN: JACSAT; ISSN: 0002-7863
 DT Journal
 LA English
 GI



AB Duocarmycin-adenine adduct (I) was isolated following alkylation of calf thymus DNA with duocarmycin. I was fully characterized by using ¹H-NMR, 2D ¹H-¹H COSY NMR, 2D ¹H-¹H NOESY NMR, and ¹³C-NMR. The data provided unambiguous assignment of the structure I in which adenine N-3 addition to the unsubstituted cyclopropane C of duocarmycin A was established.
 IT **118292-36-7**, Duocarmycin C2 **124325-94-6**, Duocarmycin B2
 RL: BIOL (Biological study)
 (DNA alkylation by, adenine adduct formation in)
 RN 118292-36-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

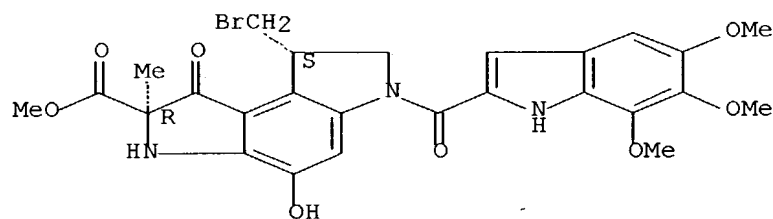
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 134781-55-8P

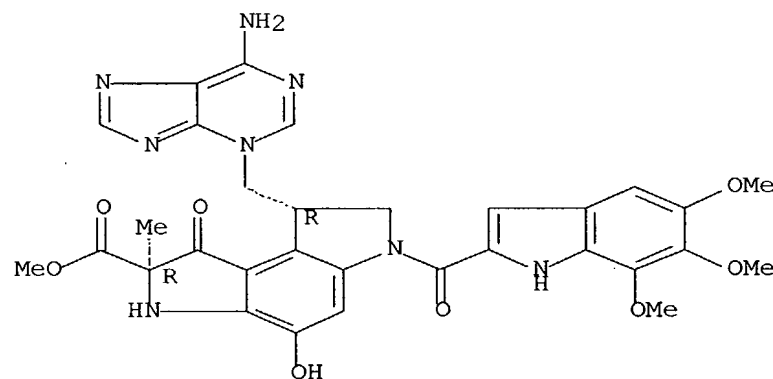
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 134781-55-8 CAPLUS

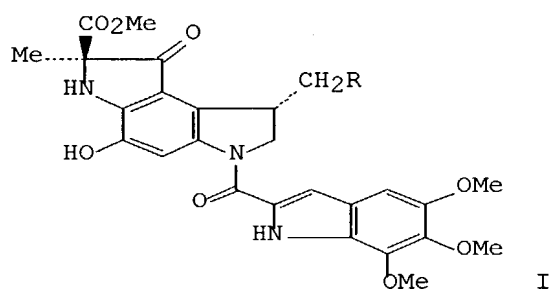
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-[(6-amino-3H-purin-3-
yl)methyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI)

(CA
INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 108 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:429824 CAPLUS Full-text
 DN 115:29824
 TI An alternative and convenient strategy for generation of substantial quantities of singly 5'-32P-end-labeled double-stranded DNA for binding studies: development of a protocol for examination of functional features of (+)-CC-1065 and the duocarmycins that contribute to their sequence-selective DNA alkylation properties
 AU Boger, Dale L.; Munk, Stephen A.; Zarrinmayeh, Hamideh; Ishizaki, Takayoshi; Haught, Joan; Bina, M.
 CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
 SO Tetrahedron (1991), 47(14-15), 2661-82
 CODEN: TETRAB; ISSN: 0040-4020
 DT Journal
 LA English
 GI



AB Development of an alternative strategy for securing substantial quantities of singly 5'-32P-end-labeled double-stranded DNA suitable for binding studies is described. The 32P label is introduced onto the free 5'-hydroxyl group of a chemical synthesized universal primer [5'-32P]-d(GTAAAACGACGGCCAGT)-3'] which is used to initiate DNA synthesis on M13-derived single-stranded DNA templates. Following DNA synthesis, a restriction enzyme cleavage reaction produces a uniform length duplex suitable for agent binding studies. The strategy further permits the use of the Sanger dideoxynucleotide sequencing technique for direct and unambiguous identification of cleavage sites introduced by an agent on the end-labeled DNA. The use of the procedure in the examination of the DNA alkylation properties of (+)-CC-1065 (I) and a series of synthetic analogs is reviewed. From these studies a refined definition of the alkylation selectivity of I is detailed. The ease with which the procedure may be extended to the rapid and convenient examination of addnl. agents is illustrated with the demonstration of the strikingly similar DNA alkylation properties of I and the duocarmycins e.g. II (R = Br, Cl), which suggest that the agents may be acting by a common

mechanism. The cytotoxicity of these alkylating agents is also discussed.

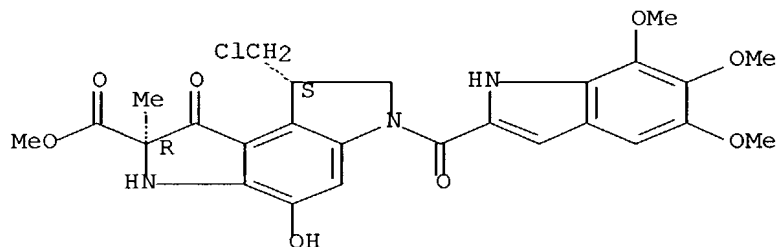
IT **118292-36-7 124325-94-6**

RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective DNA alkylation by)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

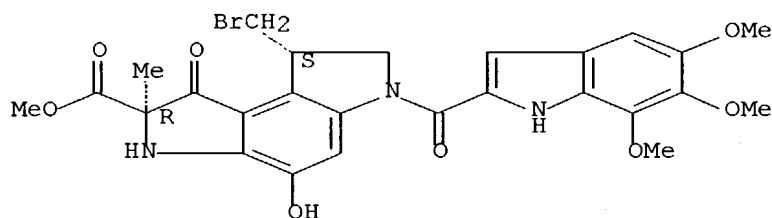
Absolute stereochemistry.



RN 124325-94-6 CAPLUS

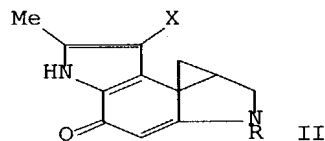
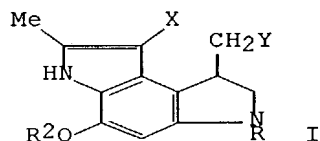
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 109 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:408427 CAPLUS Full-text
 DN 115:8427
 TI Preparation of DC-88A derivatives as antitumor agents
 IN Kanda, Yutaka; Uosaki, Youichi; Saito, Hiromitsu; Sano, Hiroshi;
 Kobayashi, Eiji; Morimoto, Makoto; Nagamura, Satoru
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 29 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 406749	A1	19910109	EP 1990-112563	19900702
	EP 406749	B1	19991027		
	R: DE, FR, GB, IT				
	JP 03128379	A2	19910531	JP 1990-168666	19900627
	JP 2510335	B2	19960626		
	US 5070092	A	19911203	US 1990-545579	19900629
	US 5187186	A	19930216	US 1991-755760	19910906
PRAI	JP 1989-171605		19890703		
	US 1990-545579		19900629		
OS	MARPAT 115:8427				
GI					



AB The title compds. (I and II; R = 5,6,7-trimethoxy-2-indolylcarbonyl; R₂ = H, alkanoyl, dialkylcarbonyl, alkoxy carbonyl, trialkylsilyl, etc.; X = H, CO₂R₁; R₁ = H, alkyl, allyl, PhCH₂; Y = Cl, Br) were prepared
 Thus, DC89B2 (fermentation preparation given) was converted in 3 steps to I (R₂ = SiMe₂CMe₃, X = CO₂Me, Y = Br) which suppressed Sarcoma 180 tumor growth in mice to 4.3 volume% that of controls 7 days after administration of 0.25 mg/kg i.v.

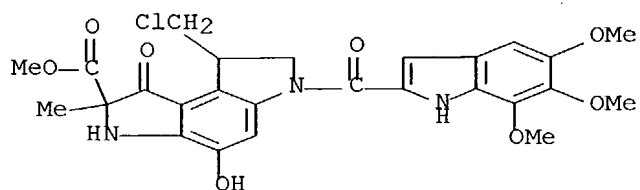
IT 134233-12-8 134233-13-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(fermentation preparation and reaction of, in preparation of antitumor agents)

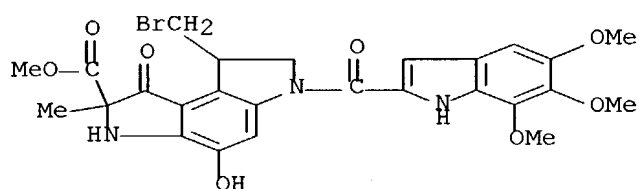
RN 134233-12-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134233-13-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



IT 129953-15-7P 134106-83-5P 134106-84-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

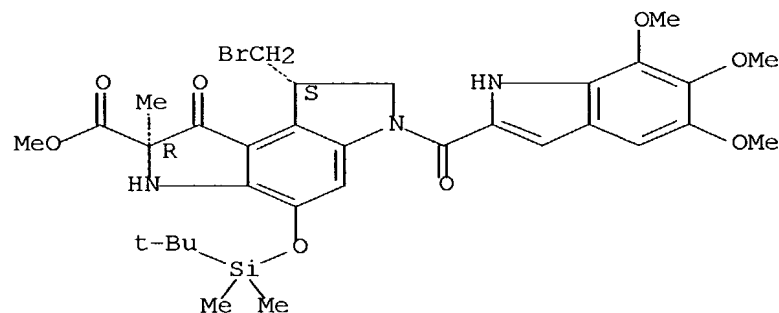
(preparation and reaction of, in preparation of antitumor agents)

RN 129953-15-7 CAPLUS

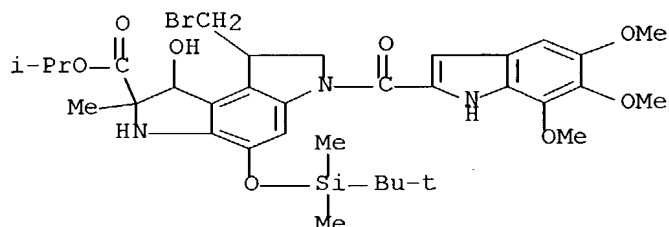
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI)

(CA INDEX NAME)

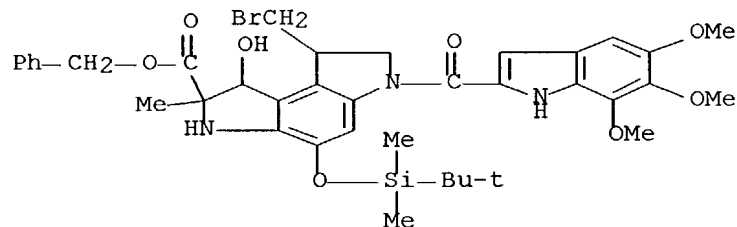
Absolute stereochemistry.



RN 134106-83-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-
 methyl-
 6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methylethyl ester (9CI)
 (CA INDEX NAME)



RN 134106-84-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-
 dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-
 methyl-
 6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester (9CI)
 (CA INDEX NAME)

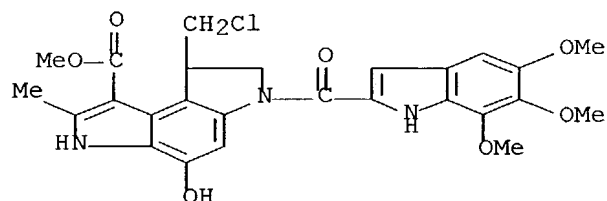


IT 134106-66-4P 134106-67-5P 134106-73-3P
 134106-74-4P 134106-75-5P 134106-76-6P
 134106-77-7P 134106-78-8P 134106-79-9P
 134106-80-2P 134106-81-3P 134106-82-4P
 134127-18-7P 134127-20-1P

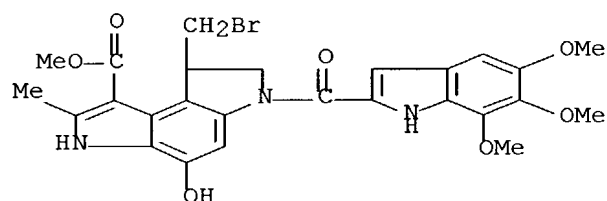
RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation)
 (preparation of, as antitumor agent)

RN 134106-66-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
 3,6,7,8-
 tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-

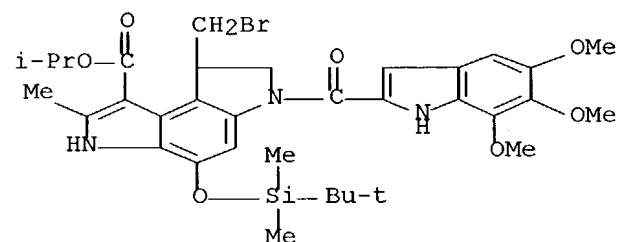
yl)carbonyl]-
 , methyl ester (9CI) (CA INDEX NAME)



RN 134106-67-5 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-
 , methyl ester (9CI) (CA INDEX NAME)

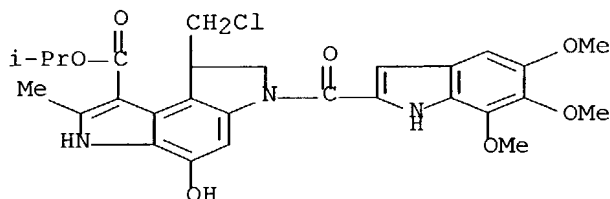


RN 134106-73-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

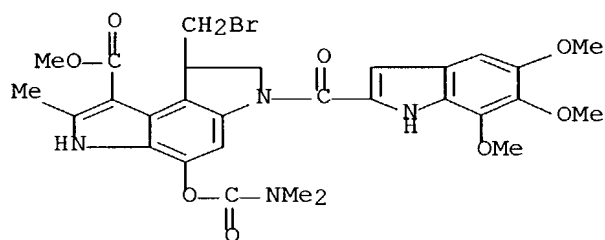


RN 134106-74-4 CAPLUS

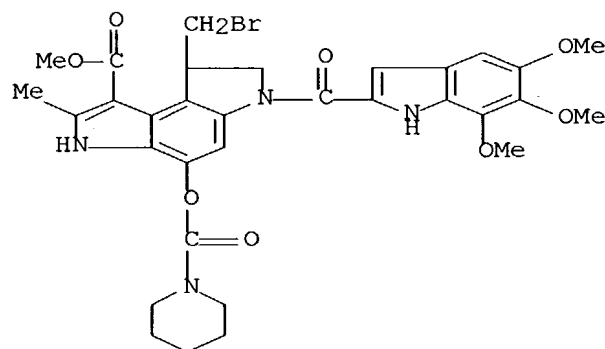
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-
3,6,7,8-
tetrahydro-4-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-
yl)carbonyl]-
, 1-methylethyl ester (9CI) (CA INDEX NAME)



RN 134106-75-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino) carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

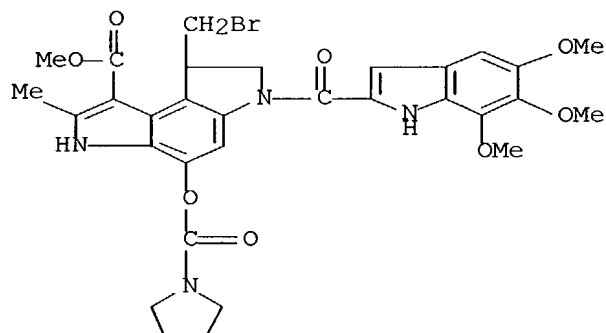


RN 134106-76-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-
1H-
indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



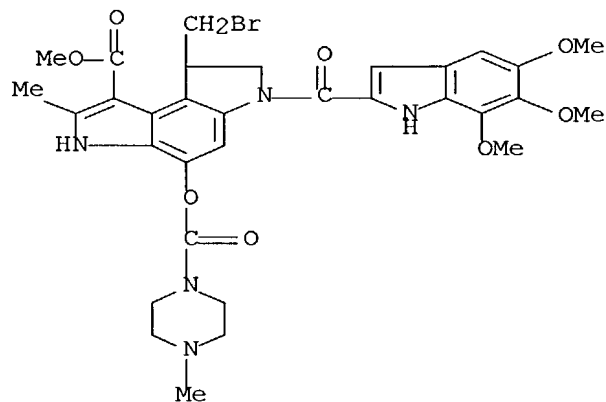
RN 134106-77-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



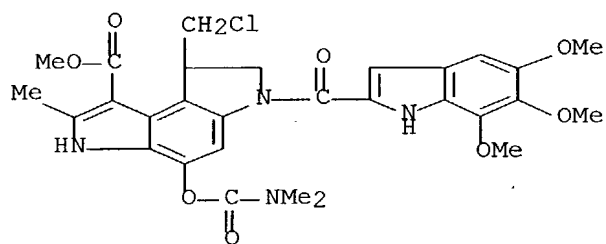
RN 134106-78-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134106-79-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

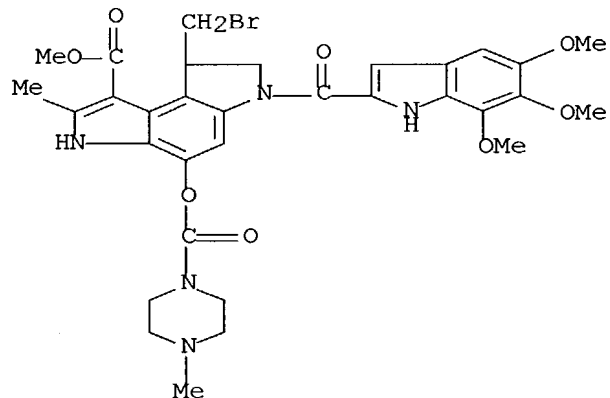


RN 134106-80-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride

(9CI)

(CA INDEX NAME)

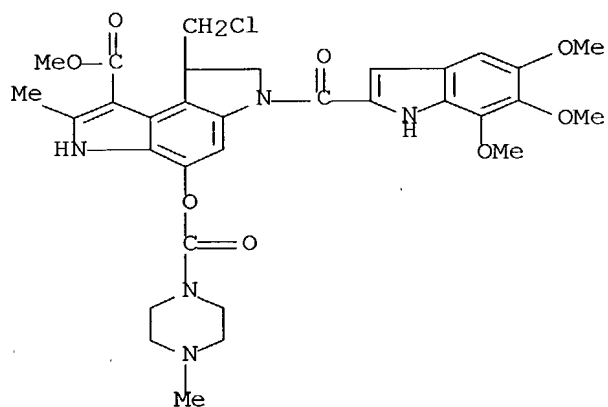


● HCl

RN 134106-81-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[4-methyl-1-piperazinyl]carbonyl]oxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



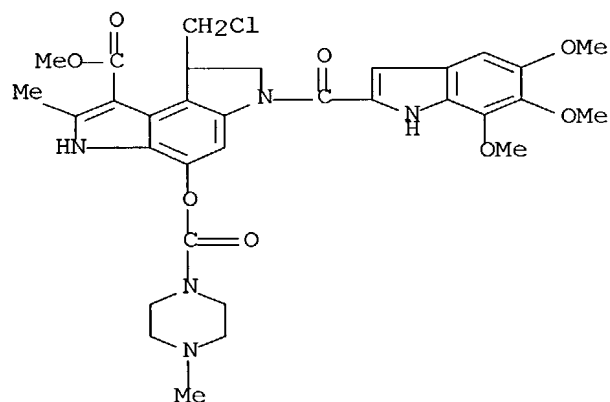
RN 134106-82-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl) carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester, monohydrochloride

(9CI)

(CA INDEX NAME)

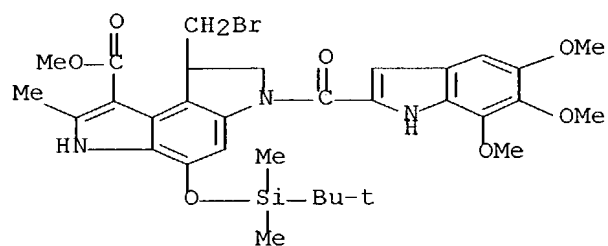


● HCl

RN 134127-18-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-

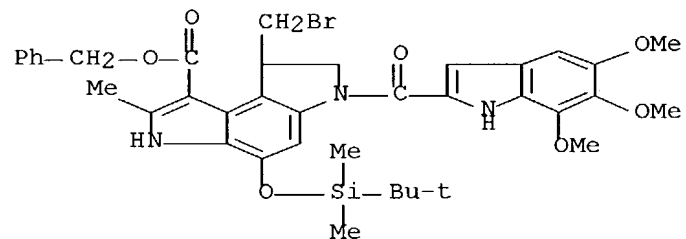
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



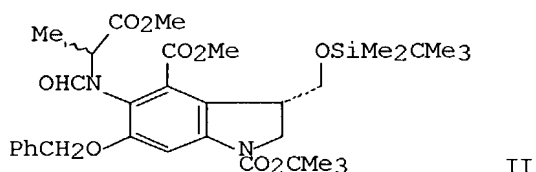
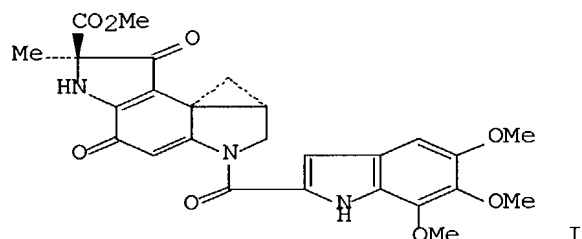
RN 134127-20-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
 [[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
 trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX
 NAME)



L10 ANSWER 110 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:142962 CAPLUS Full-text
 DN 114:142962
 TI First total synthesis of dl-duocarmycin A
 AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio; Terashima, Shiro
 CS Sagami Chem. Res. Cent., Sagamihara, 229, Japan
 SO Tetrahedron Letters (1990), 31(46), 6699-702
 CODEN: TELEAY; ISSN: 0040-4039
 DT Journal
 LA English
 OS CASREACT 114:142962
 GI



AB Synthesis of the title compound (I) was achieved by featuring introduction of a methoxycarbonyl group into the C-4 position of a 5-aminoindoline nucleus by way of an isatin derivative and subsequent ring closure to a Me 2-methylindoxyl-2-carboxylate system by the Dieckmann cyclization the indolylformamide II.

IT **132628-71-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and hydrogenolysis of)

RN 132628-71-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl) oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-

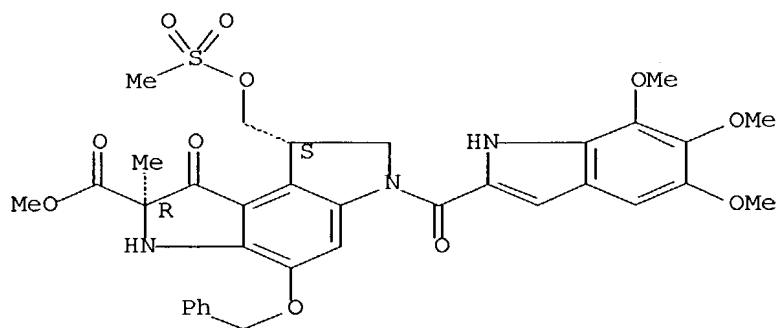
[(5,6,7-

trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA

INDEX

NAME)

Relative stereochemistry.



IT 132628-67-2P 132628-68-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

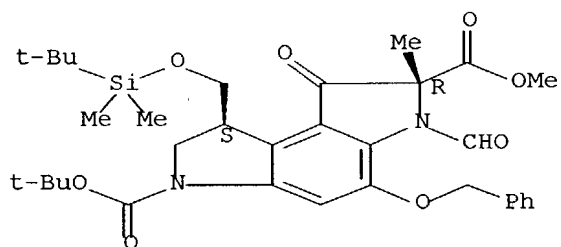
(Reactant or reagent)

(preparation and hydrolysis of)

RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, trans- (9CI) (CA INDEX NAME)

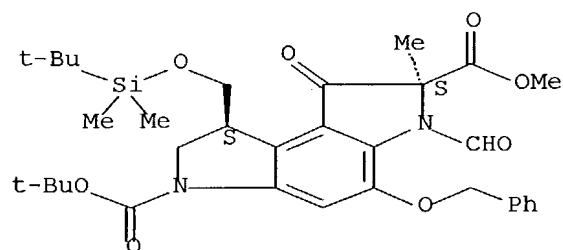
Relative stereochemistry.



RN 132628-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-
tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 132628-72-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

(Reactant or reagent)

(preparation and intramol. cyclization of)

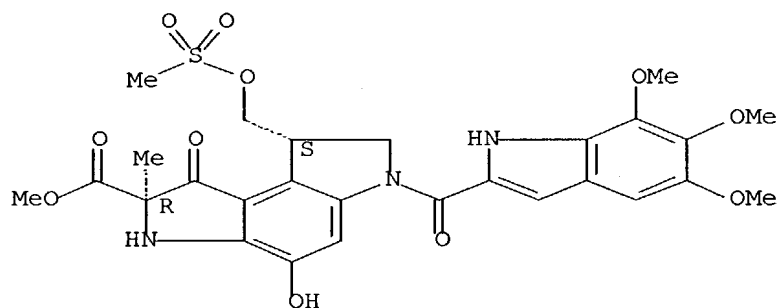
RN 132628-72-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA

INDEX

NAME)

Relative stereochemistry.



IT 132628-70-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

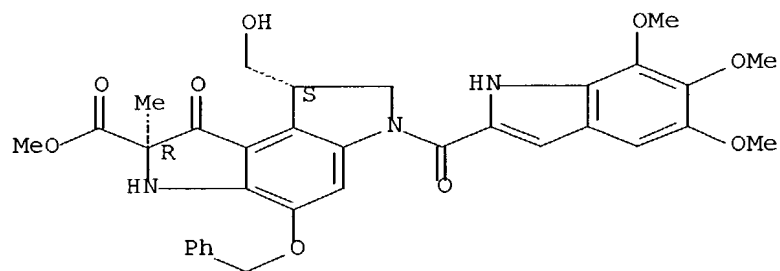
(Reactant or reagent)

(preparation and mesylation of)

RN 132628-70-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **132628-69-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT

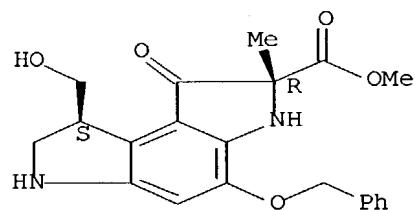
(Reactant or reagent)

(preparation and reaction of, with (dimethylaminopropyl)ethyl carbodiimide)

RN 132628-69-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, methyl ester, dihydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



●2 HCl

L10 ANSWER 111 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:23617 CAPLUS Full-text
 DN 114:23617
 TI Duocarmycin-pyrindamycin DNA alkylation properties and identification,
 synthesis, and evaluation of agents incorporating the pharmacophore of
 the
 duocarmycin-pyrindamycin alkylation subunit. Identification of the
 CC-1065 duocarmycin common pharmacophore
 AU Boger, Dale L.; Ishizaki, Takayoshi; Zarrinmayeh, Hamideh; Munk, Stephen
 A.; Kitos, Paul A.; Suntornwat, Oranart
 CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
 SO Journal of the American Chemical Society (1990), 112(24), 8961-71
 CODEN: JACSAT; ISSN: 0002-7863
 DT Journal
 LA English
 OS CASREACT 114:23617
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A demonstration and subsequent study of the DNA covalent alkylation
 properties of duocarmycin A (I) and duocarmycins C1 and C2 [pyrindamycin
 A (II) and B (III)] are detailed and have led to the identification of
 two high affinity binding sites [5'-d(A/TAAA)-3 and 5'-d(A/TTTAPu)-3']
 within a full set of available alkylation sites [5'-d(AAA)-3' > 5'-
 d(TTA)-3' > 5'-d(TAA)-3' > 5'-d(ATA)-3'] that proceeds through 3'-
 adenine N-3 alkylation of the activated cyclopropane of I similar to the
 (+)-CC-1065 covalent alkylation of DNA. The synthesis of ketone IV (CI-
 TMI) incorporating the parent 1,2,7,7a-tetrahydrocycloprop[1,2-c]indol-
 4-one (CI) alkylation subunit of I is described and the results of its
 comparative evaluation (in vitro cytotoxic activity and DNA covalent
 alkylation properties) suggest that IV constitutes an agent bearing the
 min. potent pharmacophore of DNA alkylation subunit of I and the common
 pharmacophore of the I/ML-1065 alkylation subunits.

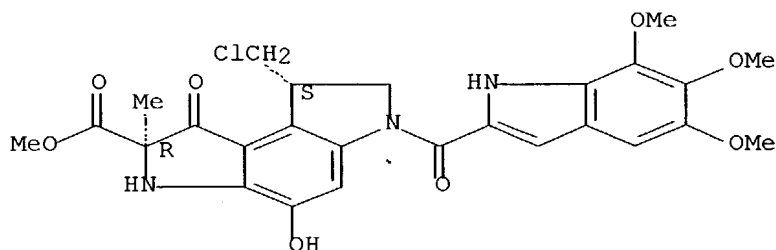
IT 118292-36-7, Pyrindamycin A

RL: RCT (Reactant); RACT (Reactant or reagent)
 (alkylation by, of DNA, binding sites for)

RN 118292-36-7 CAPLUS

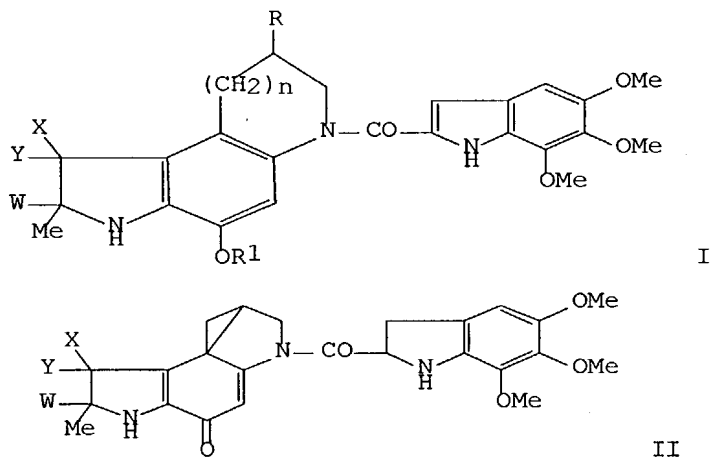
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
 indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 112 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:591321 CAPLUS Full-text
 DN 113:191321
 TI Preparation of DC-88A derivatives as antitumor agents
 IN Kanda, Yutaka; Yasuzawa, Tohru; Saito, Hiromitsu; Sano, Hiroshi;
 Kobayashi, Eiji; Morimoto, Makoto
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 39 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 365041	A1	19900425	EP 1989-119639	19891023
	EP 365041	B1	19951004		
	R: DE, FR, GB, IT				
	US 5008271	A	19910416	US 1989-423788	19891018
	JP 03007287	A2	19910114	JP 1989-272314	19891019
PRAI	JP 1988-265582		19881021		
	JP 1989-62572		19890315		
OS	MARPAT 113:191321				
GI					



AB DC-88A derivs. [I, II; R = Br, Cl, BrCH₂, ClCH₂; R₁ = H, C1-4 alkyl, C2-15 acyl, (substituted) benzoyl, dialkylcarbonyl, etc.; one of X and Y is H, the other is MeO, AcO, (substituted) PhCO₂, XY = O; W = H, allyl, (substituted) acyl, alkoxy carbonyl, alkoxy methyl, etc.; n = 0, 1] are prepared Me₃CSiMe₂Cl was added to a solution of DC-89B2 (I; R = BrCH₂, R₁ = H, W = CO₂Me, XY = O, n = 0) (preparation by culture fermentation given) and imidazole in DMF at 0° with stirring, 2N HCl was added, and the mixture extracted with EtOAc to give 95% silyl ether I (R = BrCH₂, R₁ = Me₃CSiMe₂, W = CO₂Me, XY = O, n = 0), which showed IC₅₀ of 0.010 nM

against HeLa S3 cell growth, vs. 0.039 nM with DC-88A. Also prepared were 32 addnl. I and II.

IT **130060-75-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

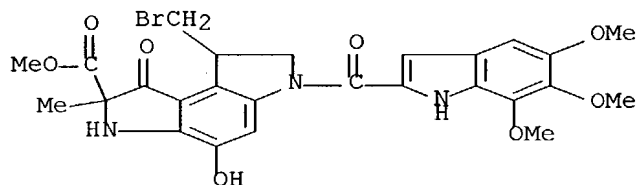
RACT

(Reactant or reagent)

(preparation and reaction of, in preparation of antitumor agents)

RN 130060-75-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



IT **129953-15-7P 129953-16-8P 129953-17-9P**

129953-18-0P 129953-19-1P 129953-20-4P

129953-21-5P 129953-22-6P 129953-23-7P

129953-24-8P 129953-25-9P 129953-26-0P

129953-27-1P 129953-28-2P 129953-29-3P

129953-31-7P 129953-32-8P 129953-33-9P

129982-35-0P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of, as antitumor agent)

RN 129953-15-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[1,1-

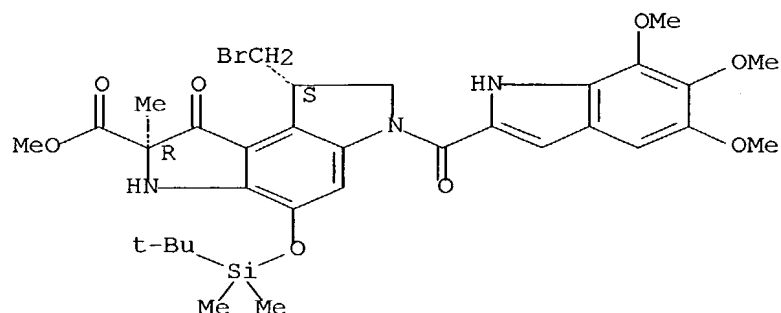
dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-

(9CI)

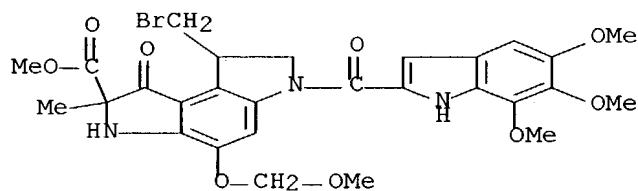
(CA INDEX NAME)

Absolute stereochemistry.



RN 129953-16-8 CAPLUS

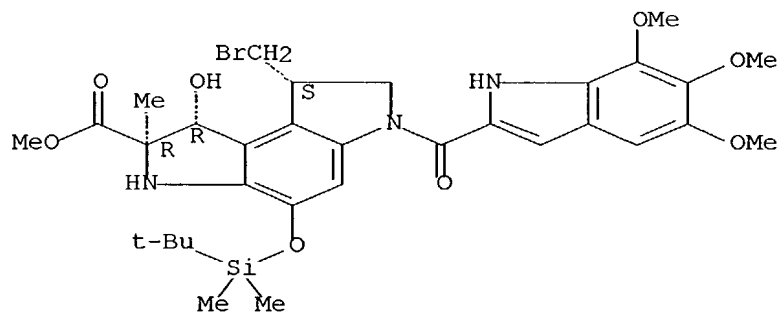
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-(methoxymethoxy)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 129953-17-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)-(9CI) (CA INDEX NAME)

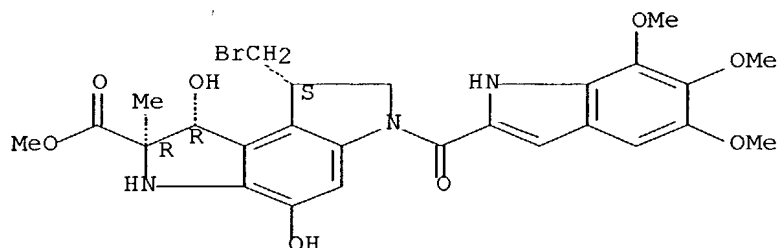
Absolute stereochemistry.



RN 129953-18-0 CAPLUS

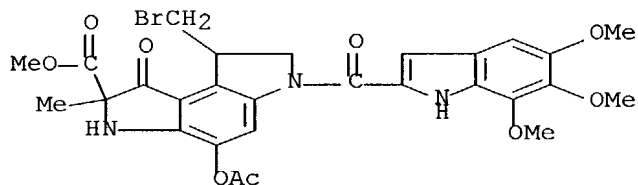
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-1,4-dihydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, [1R-(1 α ,2 β ,8 α)]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



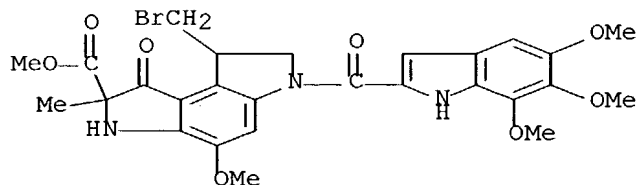
RN 129953-19-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-(acetyloxy)-8-
(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-
1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 129953-20-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-methoxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

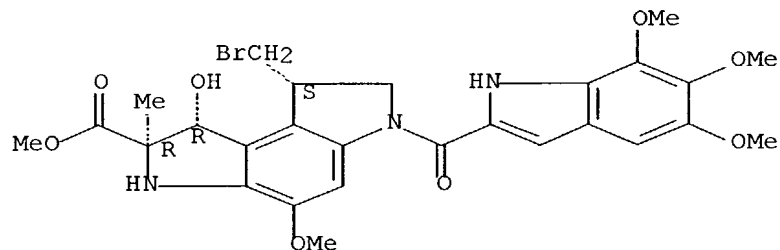


RN 129953-21-5 CAPLUS

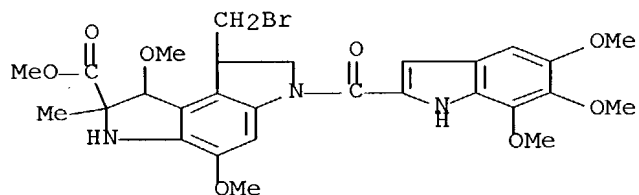
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1 α ,2 β ,8 α)]-(9CI) (CA INDEX NAME)

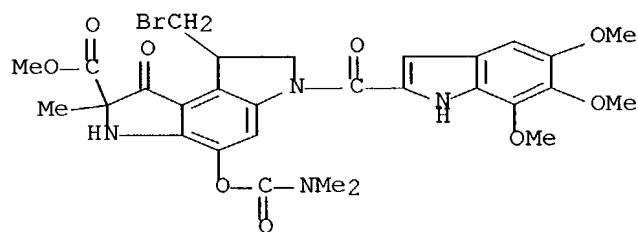
Absolute stereochemistry. Rotation (-).



RN 129953-22-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1,4-dimethoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 129953-23-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

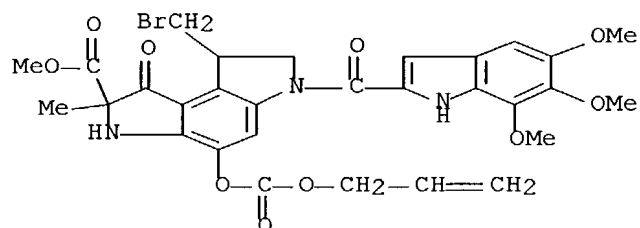


RN 129953-24-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[[(2-propenyloxy) carbonyl]oxy]-6-
[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester (9CI) (CA

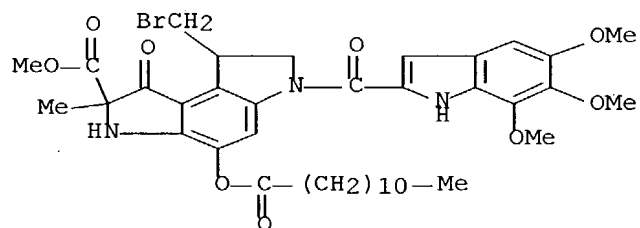
INDEX

NAME)



RN 129953-25-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-oxododecyl)oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl) carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

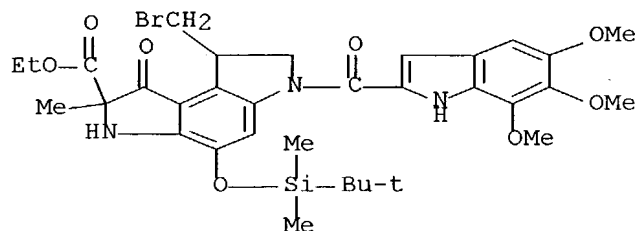


RN 129953-26-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
[(5,6,7-trimethoxy-1H-indol-2-yl) carbonyl]-, ethyl ester (9CI) (CA

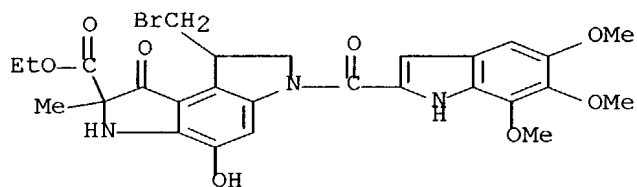
INDEX

NAME)



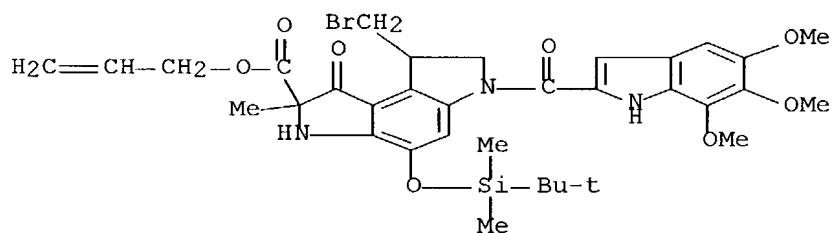
RN 129953-27-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



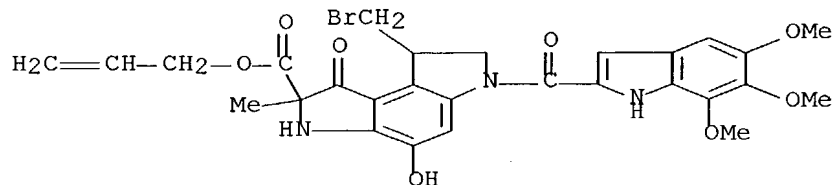
RN 129953-28-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)



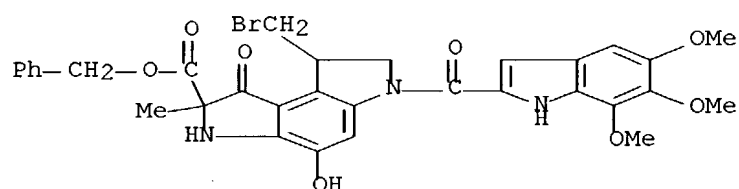
RN 129953-29-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)



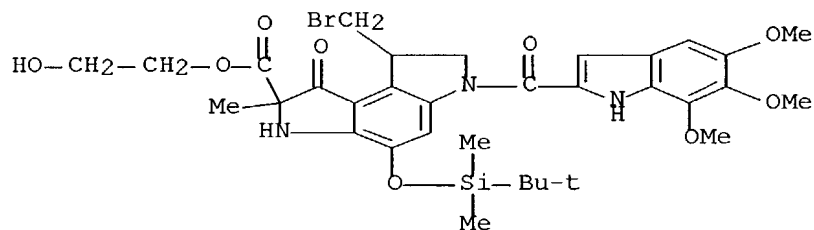
RN 129953-31-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



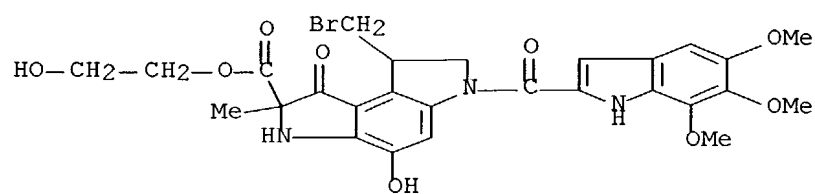
RN 129953-32-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[[1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

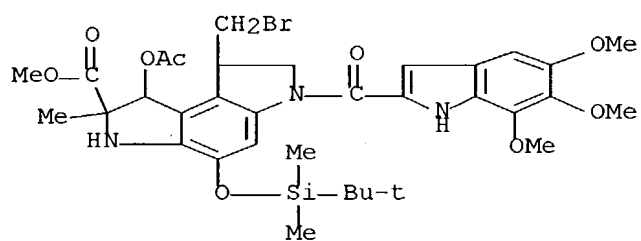


RN 129953-33-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)



RN 129982-35-0 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1-(acetyloxy)-8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 113 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:591058 CAPLUS Full-text
 DN 113:191058
 TI Preparation of antibacterial and antitumor antibiotic DC 88A
 IN Saito, Hiromitsu; Kasai, Masaji; Sano, Hiroshi; Yasuzawa, Toru;
 Ichimura,
 Michiaki; Takahashi, Keiichi
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 3 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 02115184	A2	19900427	JP 1988-265583	19881021
	JP 2553166	B2	19961113		
PRAI	JP 1988-265583		19881021		
OS	MARPAT 113:191058				
GI					

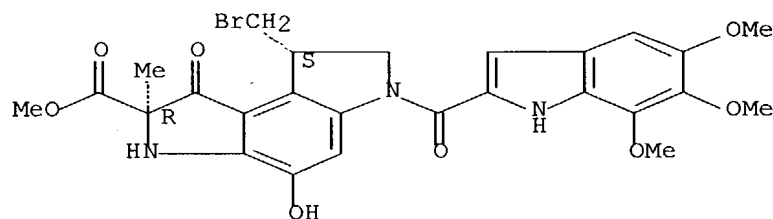
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Antibiotic DC 88A (I), useful as a antibacterial and antitumor agent (no data), is prepared by treatment of 7-hydroxyindoline derivative II (X = bond, CH₂; when X = single bond, Y = CH₂Br, CH₂Cl; when X = CH₂, Y = Br, Cl) with bases or Ag salts. A solution of II (X = CH₂, Y = Br) in MeCN was treated with DBU at room temperature for 45 min to give 83% I.

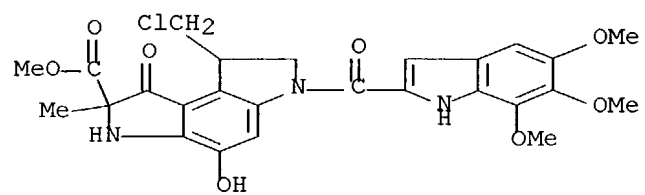
IT **124325-94-6 128517-09-9**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (intramol. dehydrohalogenation of, antibiotic DC 88A from)

RN 124325-94-6 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 128517-09-9 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 114 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:552150 CAPLUS Full-text
 DN 113:152150
 TI Preparation of DC-88A derivatives as antitumor agents
 IN Saito, Hiromitsu; Kasai, Masaji; Morimoto, Makoto; Kobayashi, Eiji;
 Uosaki, Yoichi; Kanda, Yutaka; Sano, Hiroshi
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 45 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 354583	A1	19900214	EP 1989-114896	19890811
	EP 354583	B1	19931103		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 02288879	A2	19901128	JP 1989-206170	19890809
	US 5084468	A	19920128	US 1989-392271	19890810
	AT 96797	E	19931115	AT 1989-114896	19890811
	US 5117006	A	19920526	US 1991-700507	19910515
PRAI	JP 1988-200352		19880811		
	JP 1988-265581		19881021		
	JP 1989-34482		19890214		
	US 1989-392271		19890810		
	EP 1989-114896		19890811		

OS MARPAT 113:152150

GI For diagram(s), see printed CA Issue.

AB The title compds. [I and II; R = H, (un)substituted (phenyl)alkanoyl, heterocyclylcarbonyl, etc.; X = Cl, Br, iodo; when m = 0, n = 0] were prepared Thus, DC-88A (I; R = 5,6,7-trimethoxyindolylcarbonyl) was deacylated with NaOMe in MeOH and the product condensed with 4-nitrophenyl 5-methoxyindole-2-carboxylate to give I (R = 5-methoxyindolylcarbonyl) which had IC₅₀ of 0.0034 nM against HeLa S3 cells in vitro.

IT **128438-86-8P 128438-88-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

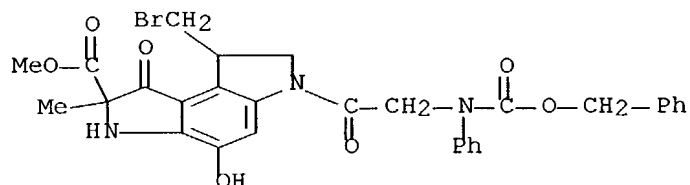
RACT

(Reactant or reagent)

(preparation and reaction of, in preparation of antitumor agents)

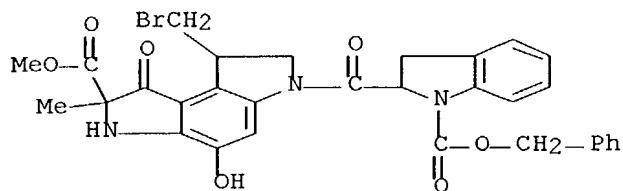
RN 128438-86-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-
 [[phenyl[(phenylmethoxy)carbonyl]amino]acetyl]-, methyl ester (9CI) (CA
 INDEX NAME)



RN 128438-88-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[[2,3-dihydro-1-[(phenylmethoxy)carbonyl]-1H-indol-2-yl]carbonyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



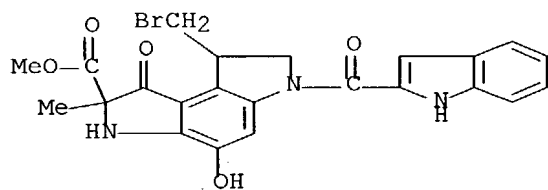
IT 128438-14-2P 128438-15-3P 128438-16-4P
128438-17-5P 128438-19-7P 128438-21-1P
128438-23-3P 128438-25-5P 128438-29-9P
128438-30-2P 128438-33-5P 128438-35-7P
128438-37-9P 128438-39-1P 128438-40-4P
128438-42-6P 128438-43-7P 128438-44-8P
128438-45-9P 128438-46-0P 128438-47-1P
128438-48-2P 128438-49-3P 128438-50-6P
128438-51-7P 128438-52-8P 128438-53-9P
128438-54-0P 128438-55-1P 128438-56-2P
128438-57-3P 128454-34-2P 128454-35-3P
128454-36-4P 128454-37-5P 129742-14-9P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation of, as antitumor agent)

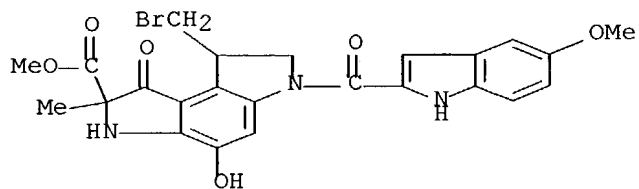
RN 128438-14-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-(1H-indol-3-ylcarbonyl)-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



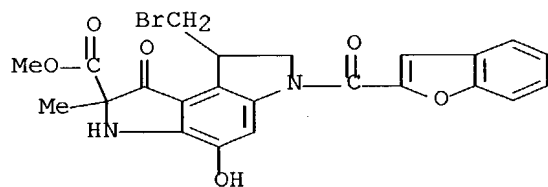
RN 128438-15-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[(5-methoxy-1H-indol-2-yl)carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



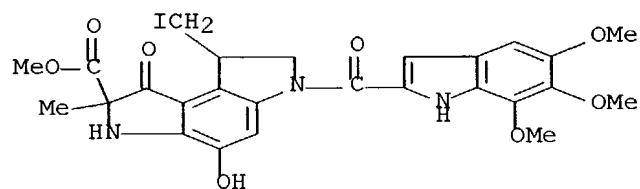
RN 128438-16-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-(2-benzofuranylcarbonyl)-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



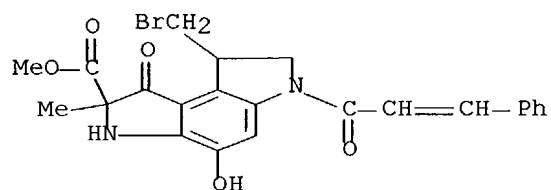
RN 128438-17-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-8-(iodomethyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-19-7 CAPLUS

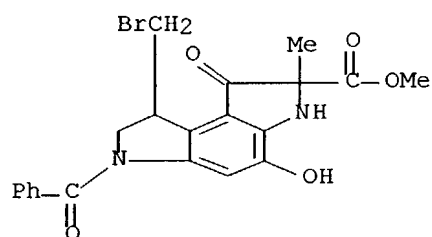
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-(1-oxo-3-phenyl-2-propenyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-21-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-benzoyl-8-(bromomethyl)-

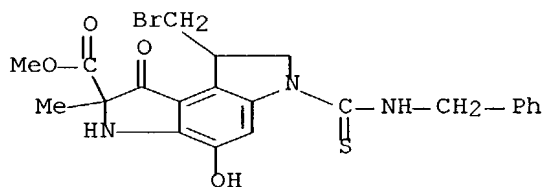
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-23-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-

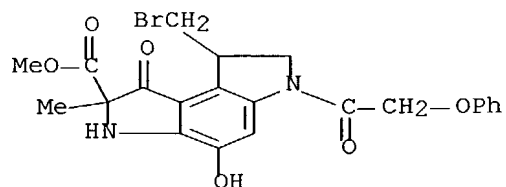
[[[(phenylmethyl)amino]thioxomethyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-25-5 CAPLUS

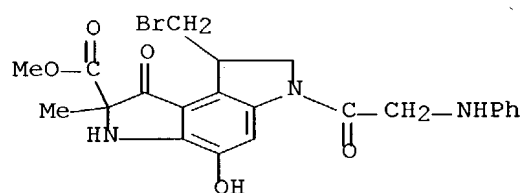
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-(phenoxyacetyl)-,

methyl ester (9CI) (CA INDEX NAME)



RN 128438-29-9 CAPLUS

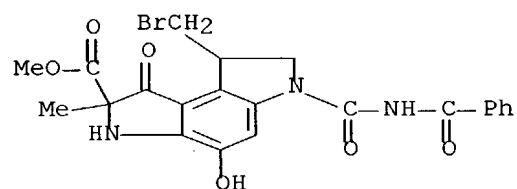
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(phenylamino)acetyl]-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

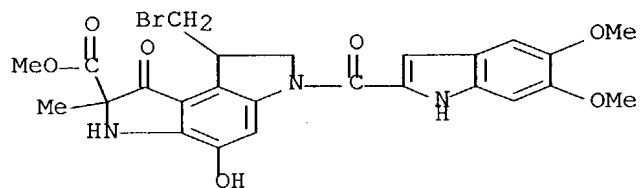
RN 128438-30-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[(benzoylamino)carbonyl]-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



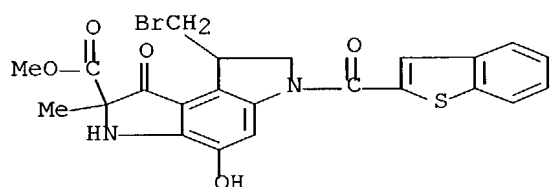
RN 128438-33-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[(5,6-dimethoxy-1H-indol-2-yl)carbonyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



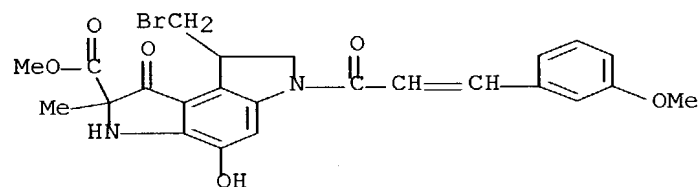
RN 128438-35-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-(benzo[b]thien-2-ylcarbonyl)-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



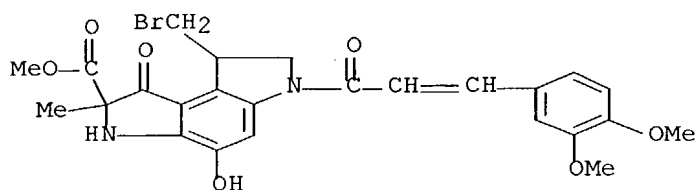
RN 128438-37-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-(3-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-39-1 CAPLUS

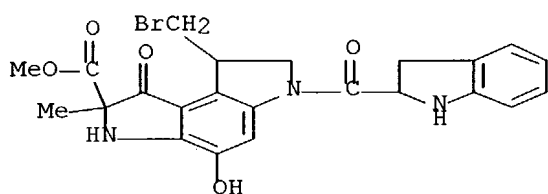
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[3-(3,4-dimethoxyphenyl)-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-40-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[(2,3-dihydro-1H-indol-2-yl)carbonyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-

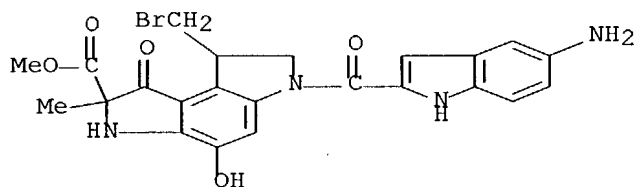
oxo-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 128438-42-6 CAPLUS

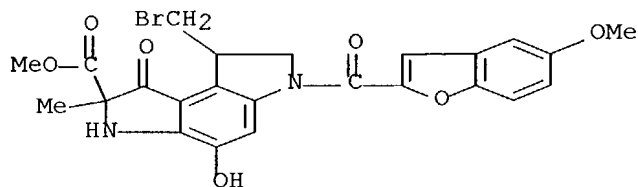
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[(5-amino-1H-indol-2-yl)carbonyl]-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-43-7 CAPLUS

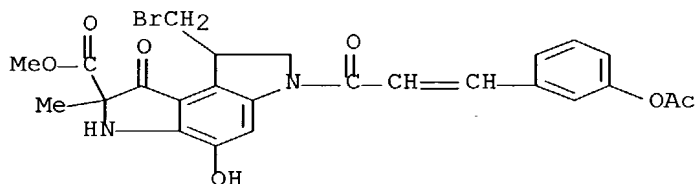
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-

methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



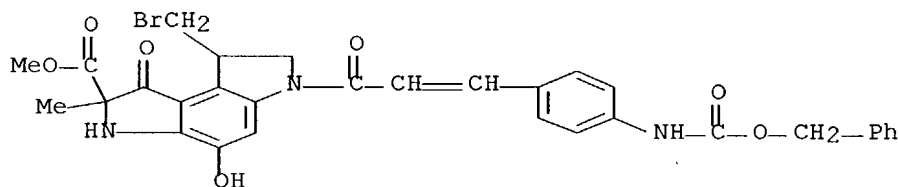
RN 128438-44-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-[3-(1-oxo-2-propenyl)-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)]-1-oxo-2-propenyl]-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



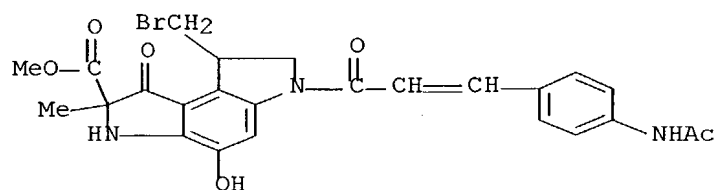
RN 128438-45-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[1-oxo-3-[4-[(phenylmethoxy)carbonyl]amino]phenyl]-2-propenyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-46-0 CAPLUS

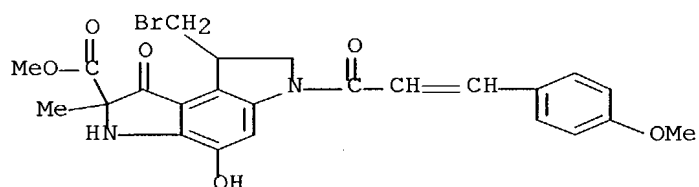
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-[4-(acetylamino)phenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-47-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-

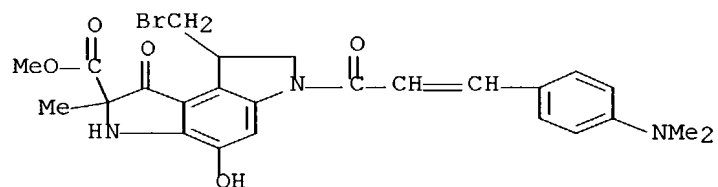
methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-48-2 CAPLUS

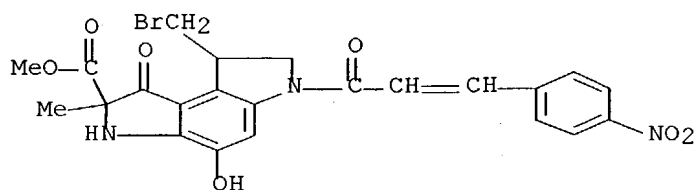
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-

methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



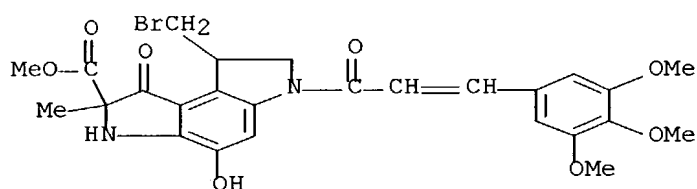
RN 128438-49-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-6-[3-(4-nitrophenyl)-1-oxo-2-propenyl]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



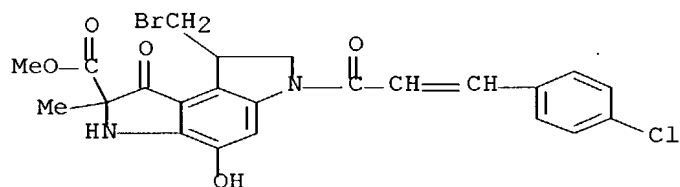
RN 128438-50-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[1-oxo-3-(3,4,5-trimethoxyphenyl)-2-propenyl]-, methyl ester (9CI) (CA INDEX NAME)



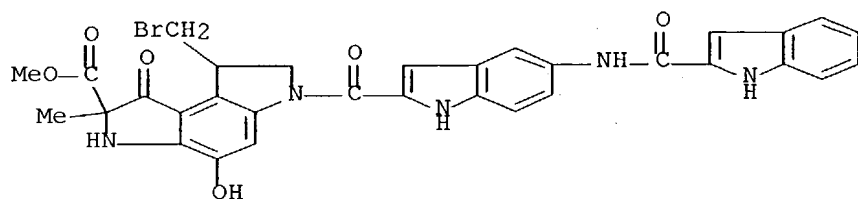
RN 128438-51-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[3-(4-chlorophenyl)-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



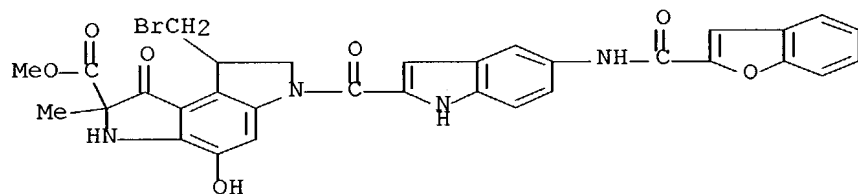
RN 128438-52-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



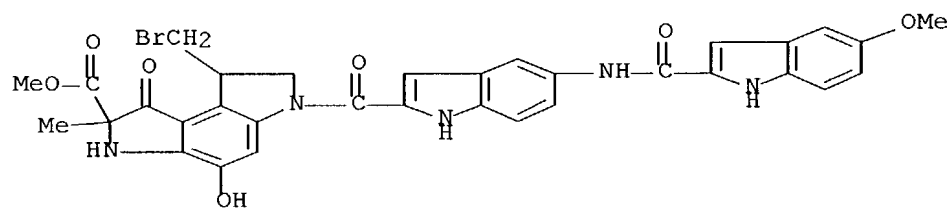
RN 128438-53-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



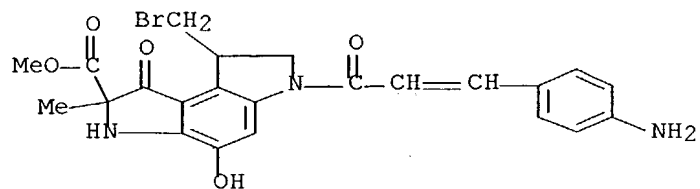
RN 128438-54-0 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[[5-[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



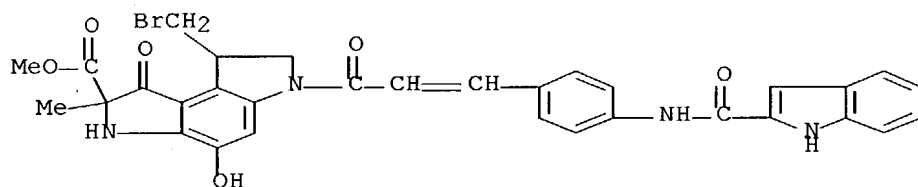
RN 128438-55-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-(4-aminophenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



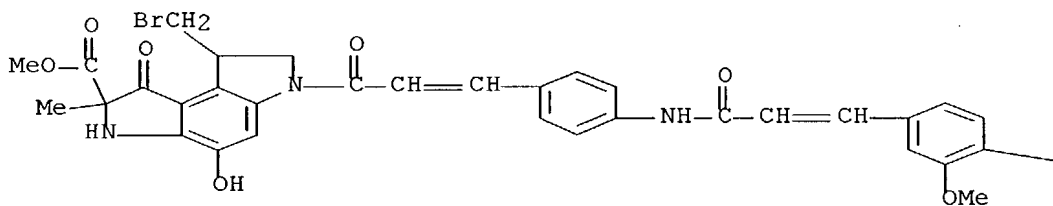
RN 128438-56-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-6-[3-[4-[(1H-indol-2-ylcarbonyl)amino]phenyl]-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128438-57-3 CAPLUS

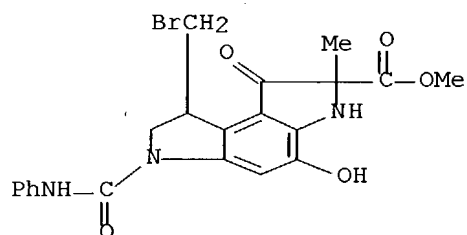
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[3-[4-[[3-(3,4-dimethoxyphenyl)-1-oxo-2-propenyl]amino]phenyl]-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-6-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



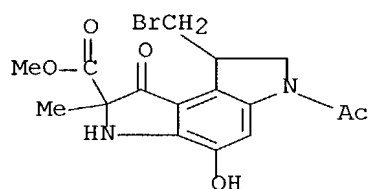
PAGE 1-A

—OMe

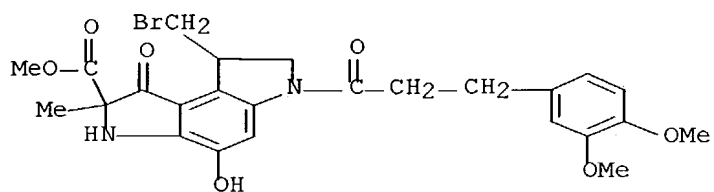
RN 128454-34-2 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-
 [(phenylamino)carbonyl]-,
 methyl ester (9CI) (CA INDEX NAME)



RN 128454-35-3 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-8-
 (bromomethyl)-
 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA
 INDEX NAME)



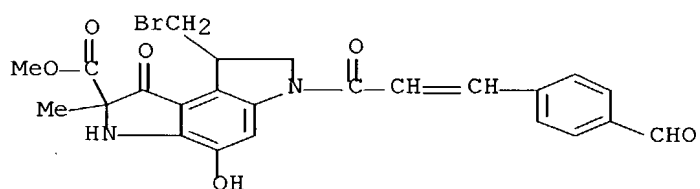
RN 128454-36-4 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[3-
 (3,4-
 dimethoxyphenyl)-1-oxopropyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-
 1-
 oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 128454-37-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[3-(4-formylphenyl)-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-

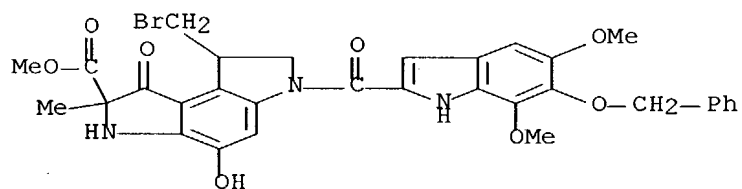
oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 129742-14-9 CAPLUS

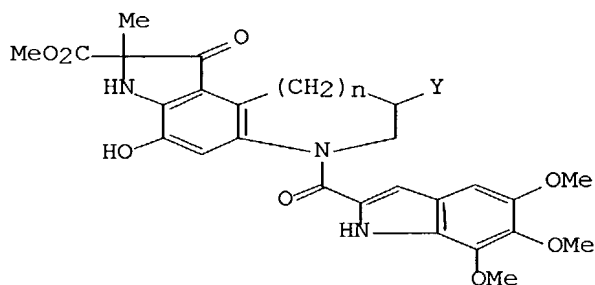
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[[5,7-dimethoxy-6-(phenylmethoxy)-1H-indol-2-yl]carbonyl]-1,2,3,6,7,8-hexahydro-

4-hydroxy-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 115 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:476608 CAPLUS Full-text
 DN 113:76608
 TI DC-89 compounds and process for their preparation
 IN Takahashi, Keiichi; Ichimura, Michio; Katsumata, Shigeo; Ogawa, Tatsuhiko;
 Morimoto, Makoto; Ashizawa, Tadashi; Kasai, Masaji; Muroi, Kenichi; Saito, Hiromitsu; et al.
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 16 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 351865	A2	19900124	EP 1989-113431	19890721
	EP 351865	A3	19900627		
	EP 351865	B1	19950503		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 02119787	A2	19900507	JP 1988-265580	19881021
	JP 2642165	B2	19970820		
	US 5138059	A	19920811	US 1989-380379	19890717
	AT 122045	E	19950515	AT 1989-113431	19890721
PRAI	JP 1988-182866		19880722		
	JP 1988-265580		19881021		
OS	MARPAT 113:76608				
GI					



I, $n=0$, $Y=CH_2Cl$
 II, $n=1$, $Y=Br$
 III, $n=0$, $Y=CH_2Br$

AB Three new antibiotics, designated DC-89A2 (I), DC-89B1 (II), and DC-89B2 (III), were produced by *Streptomyces*. Thus *S. lydicus* was cultivated in a production medium containing 5% maltose, 1.5% dry yeast, 2.5% Ebios, 1% KCl, and small amts. of KH_2PO_4 , $MgSO_4$, and $CaCO_3$, pH 5.0. After 100 h of fermentation, I was isolated from the cells and culture filtrate by extraction with $PrOH$ followed by adsorption on Diaion HP-20, and then eluted with $MeOH$, concentrated, and recrystd. from $MeOH$ to give 1.0 g of pure I. I, II, and III had low toxicity and high antibacterial as well as antitumor activities.

IT 124325-94-6, DC 89B2 128517-09-9, DC 89A2

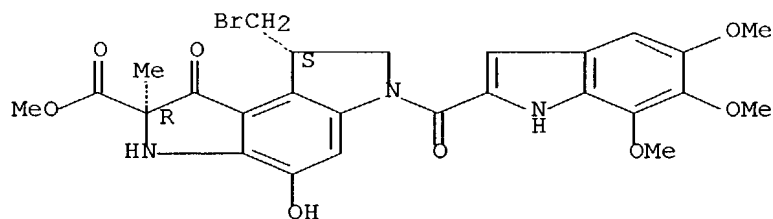
RL: BIOL (Biological study)

(antitumor antibiotic, from *Streptomyces lydicus*)

RN 124325-94-6 CAPLUS

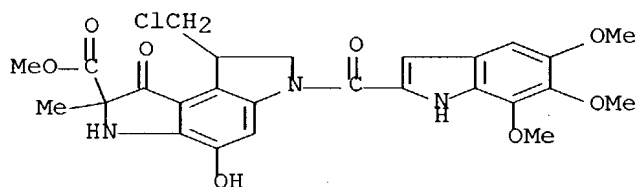
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



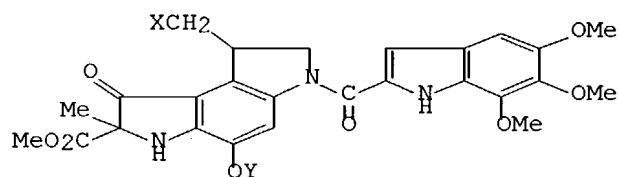
RN 128517-09-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 116 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:197974 CAPLUS Full-text
 DN 112:197974
 TI Preparation of antitumor antibiotic SF2582C derivatives
 IN Koyama, Masao; Ohba, Kazunori; Nakazawa, Tadashi; Yamamoto, Haruo;
 Sezaki,
 Masaji; Kondo, Shinichi
 PA Meiji Seika Kaisha, Ltd., Japan
 SO Eur. Pat. Appl., 7 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 339681	A2	19891102	EP 1989-107799	19890428
	EP 339681	A3	19900131		
	EP 339681	B1	19930331		
	R: DE, FR, GB				
	JP 01275581	A2	19891106	JP 1988-103782	19880428
	JP 2562935	B2	19961211		
PRAI	JP 1988-103782		19880428		
OS	MARPAT 112:197974				
GI					



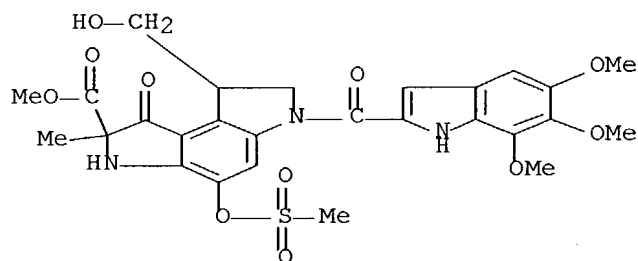
I

AB Antibiotic SF2582C derivs. (I; X, Y = RSO₂; R = tolyl, Me, OH, H; excluding X = Y = X) are prepared, having an intense antitumor activity, while the parent antibiotic SF2582C lacks the antitumor activity. Thus, 40 mg antibiotic SF2582C (II) (isolated from a Streptomyces SF2582 strain) was treated with (MeSO₂)₂O in DMF containing Et₃N to give, after silica gel chromatog., 41 mg I (X = Y = MeSO₂) (III) and 6.3 mg II monomethanesulfonate (IV). III and IV increased the life span of mice transplanted with P-388 tumor cells by 54% at 21 mg/kg and 40% at 1 mg/kg, resp.

IT **126590-90-7P 126590-91-8P 126639-63-2P**
126641-01-8P 126641-02-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation of, as antitumor agent)

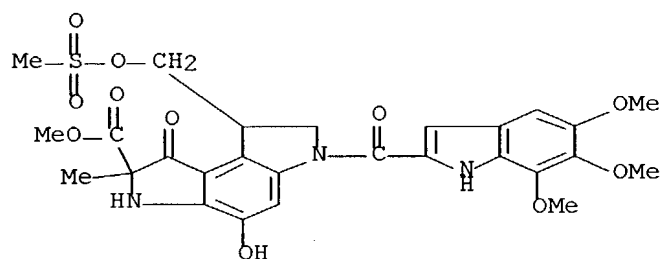
RN 126590-90-7 CAPLUS
 CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-

trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 126590-91-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



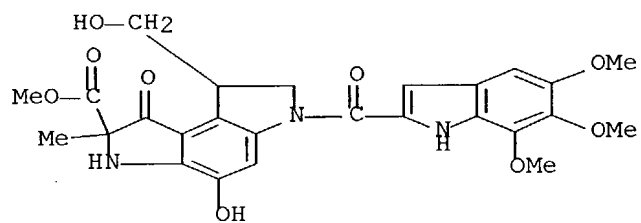
RN 126639-63-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-7-carboxylic acid, 1,2,3,6,7,8-hexahydro-5-hydroxy-1-(hydroxymethyl)-7-methyl-8-oxo-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, mono(4-methylbenzenesulfonate) (ester) (9CI)
(CA INDEX NAME)

CM 1

CRN 125600-37-5

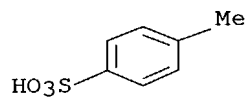
CMF C26 H27 N3 O9



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



RN 126641-01-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-7-carboxylic acid, 1,2,3,6,7,8-hexahydro-5-hydroxy-1-(hydroxymethyl)-7-methyl-8-oxo-3-[(5,6,7-trimethoxy-1H-indol-

2-yl)carbonyl]-, methyl ester, hydrogen sulfate (ester), compd. with pyridine (9CI) (CA INDEX NAME)

CM 1

CRN 110-86-1

CMF C5 H5 N



CM 2

CRN 126641-00-7

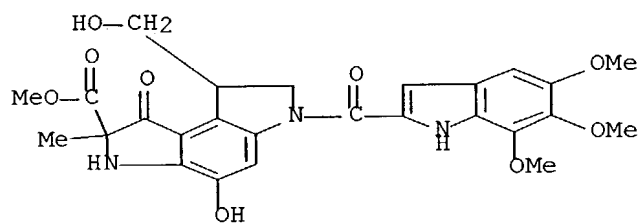
CMF C26 H27 N3 O12 S

CCI IDS

CM 3

CRN 125600-37-5

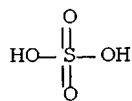
CMF C26 H27 N3 O9



CM 4

CRN 7664-93-9

CMF H2 O4 S



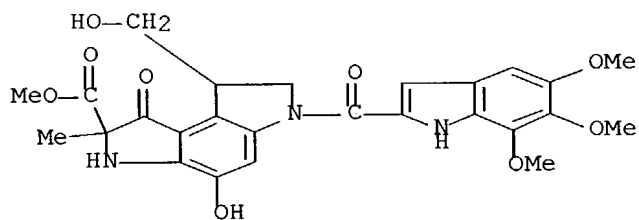
RN 126641-02-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-7-carboxylic acid, 1,2,3,6,7,8-hexahydro-5-hydroxy-1-(hydroxymethyl)-7-methyl-8-oxo-3-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, methanesulfonate (ester) (9CI) (CA INDEX NAME)

CM 1

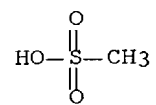
CRN 125600-37-5

CMF C26 H27 N3 O9



CM 2

CRN 75-75-2
CMF C H4 O3 S



L10 ANSWER 117 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:117334 CAPLUS Full-text

DN 112:117334

TI Manufacture of novel antitumor antibiotic substances with Streptomyces

IN Ohba, Kazunori; Watabe, Hiroomi; Nagasawa, Mieko; Sakakibara, Shiro;
Shomura, Takashi; Sezaki, Masaji; Kondo, Shinishi

PA Meiji Seika Kaisha, Ltd., Japan

SO Eur. Pat. Appl., 29 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	EP 318056	A2	19890531	EP 1988-119835	19881128
	EP 318056	A3	19901219		
	R: DE, FR, GB				
	JP 01139590	A2	19890601	JP 1987-297476	19871127
	JP 01265890	A2	19891023	JP 1988-94544	19880419
PRAI	JP 1987-297476		19871127		
	JP 1988-94544		19880419		

AB Novel antibiotics SF2582-A, SF2582-B, and SF2582-C are produced with Streptomyces SF2582. These antibiotics also have antitumor activity. The described strain was cultured for 5 days at 28° in 1000 L medium. After addition of diatomaceous earth, the mixture was filtered to obtain a cake which was extracted with aqueous Me₂CO. The Me₂CO extract was concentrated and extracted with EtOAC, and this extract was concentrated and extracted with hexane. The hexane-insol. matter was chromatographed on silica gel and Sephadex LH-20 to prepare crude SF2582-A and -B. SF2582-A 182 mg was prepared by preparative layer chromatog., and SF2582-B by preparative layer chromatog. and Toyopearl HW-40 column chromatog. SF2582-C 450 mg were prepared from a similar cake by a similar procedure. The antibiotics were characterized by UV, IR, ¹H- and ¹³C-NMR spectra; by their antimicrobial activity (e.g. the min. inhibitory concentration of SF2582-A against Staphylococcus aureus and S. epidermidis was <0.025, and against Enterococcus faecalis and Bacillus anthracis 0.05 µg/mL); and by their antitumor activity (e.g., i.p. administered SF2582-A improved the survival of P-388 tumor cell-containing mice by .apprx.50% at 0.13 mg/kg).

IT **118292-36-7P**, Antibiotic SF 2582A **125600-37-5P**,
Antibiotic SF 2582C

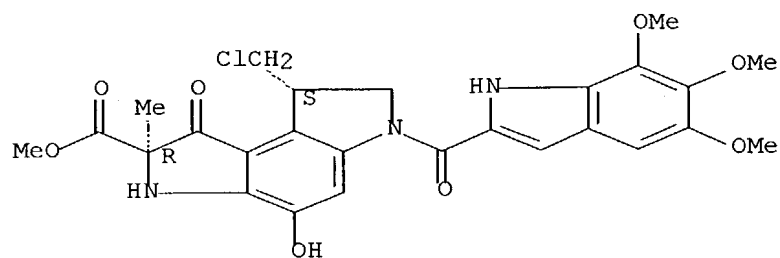
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP
(Preparation)

(manufacture of, with Streptomyces, as neoplasm inhibitor)

RN 118292-36-7 CAPLUS

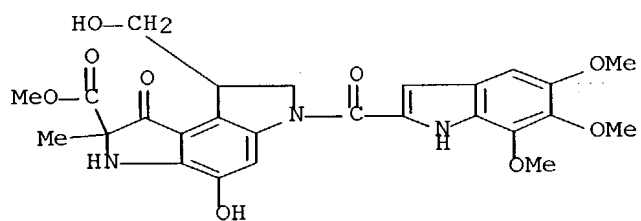
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-
1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-
indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

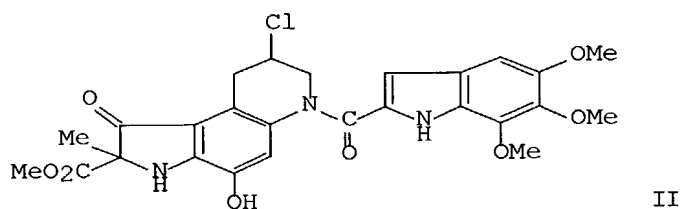
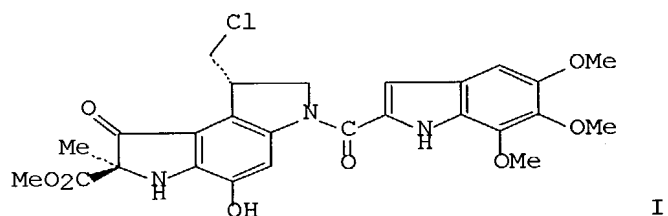


RN 125600-37-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-4-hydroxy-8-(hydroxymethyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

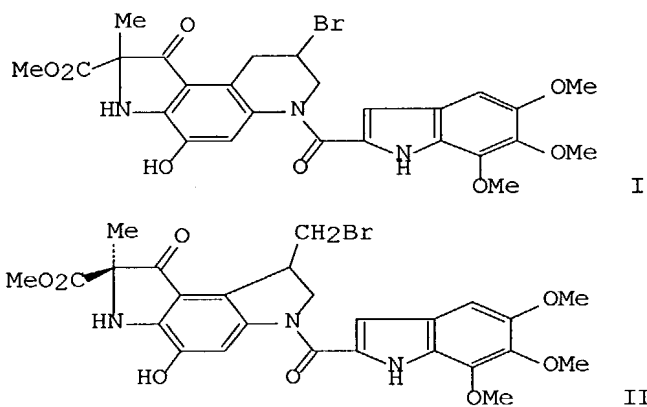


L10 ANSWER 118 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:69500 CAPLUS Full-text
 DN 112:69500
 TI Antitumor activity of pyrindamycins A and B
 AU Ishii, Shigetaka; Nagasawa, Mieko; Kariya, Yuko; Yamamoto, Haruo;
 Inouye,
 Shigeharu; Kondo, Shinichi
 CS Pharm. Res. Lab., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan
 SO Journal of Antibiotics (1989), 42(11), 1713-17
 CODEN: JANTAJ; ISSN: 0021-8820
 DT Journal
 LA English
 GI



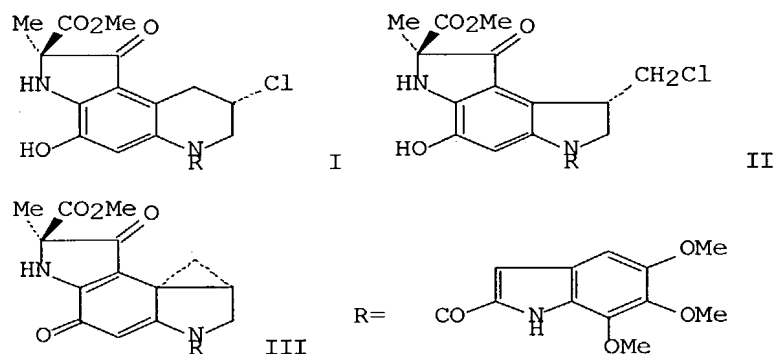
AB Pyrindamycins A (I) and B (II) exhibited stronger cytotoxic activities than doxorubicin towards murine and human tumor cell lines and especially towards doxorubicin-resistant cells. Pyrindamycins A and B were also active in vivo against P388/ADR, a multidrug-resistant tumor cell line. Intracellular accumulation of pyrindamycins A and B in P388/ADR was the same as in P388. These antibiotics strongly inhibited DNA synthesis compared with RNA or protein synthesis. They showed significant therapeutic effects towards murine leukemia, but not to solid tumors.

L10 ANSWER 119 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:18621 CAPLUS Full-text
DN 112:18621
TI New antitumor antibiotics, duocarmycins B1 and B2
AU Ogawa, Tatsuhiro; Ichimura, Michio; Katsumata, Shigeo; Morimoto, Makoto;
Takahashi, Keiichi
CS Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan
SO Journal of Antibiotics (1989), 42(8), 1299-301
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



AB Streptomyces DO-89 produced duocarmycins B1 (I) and B2 (II), which were purified by solvent extraction and chromatog. II was crystallized The phys. properties and NMR data for I and II are tabulated. I and II were potent inhibitors of sarcoma 180 in mice.

L10 ANSWER 120 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1989:231306 CAPLUS Full-text
 DN 110:231306
 TI Structure determination of novel antitumor antibiotic duocarmycins
 AU Yasuzawa, T.; Sano, H.; Iida, T.; Takahashi, I.; Muroi, K.; Ichimura, M.;
 Ogawa, T.; Takahashi, K.
 CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan
 SO Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1988), 30, 300-7
 CODEN: TYKYDS
 DT Journal
 LA Japanese
 GI



AB The structures of duocarmycin Cl (I), C2 (II), and A (III) were detd by ¹H NMR spectra, by observation of ¹H-¹³C long range couplings through COLOC spectra, and chemical reaction data. Treatment of III with HCL in acetone gave I and II in the ratio .apprx.1:4. Thus, I and II seemed to be artifact products of III.

L10 ANSWER 121 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1989:72198 CAPLUS Full-text

DN 110:72198

TI Pyrindamycins A and B, new antitumor antibiotics

AU Ohba, Kazunori; Watabe, Hiroomi; Sasaki, Toru; Takeuchi, Yasuo; Kodama, Yoshio; Nakazawa, Tadashi; Yamamoto, Haruo; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi

CS Res. Lab., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan

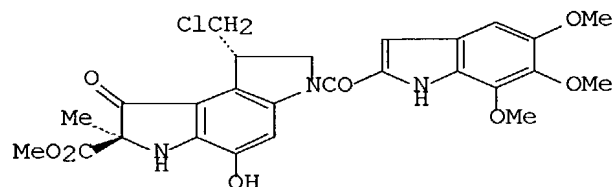
SO Journal of Antibiotics (1988), 41(10), 1515-19

CODEN: JANTAJ; ISSN: 0021-8820

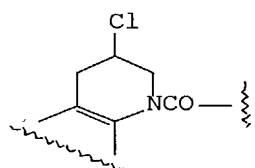
DT Journal

LA English

GI



I



II

AB Pyrindamycins A (I) and B (II) were isolated from the culture broth of *Streptomyces* sp. SF2582, their structures were determined and they exhibited activity against both gram-pos. and -neg. bacteria. Marked increases in life span were observed with single i.p. treatment of I and II against mice i.p. implanted with P388 leukemia.

IT 118292-36-7

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); BIOL (Biological study)

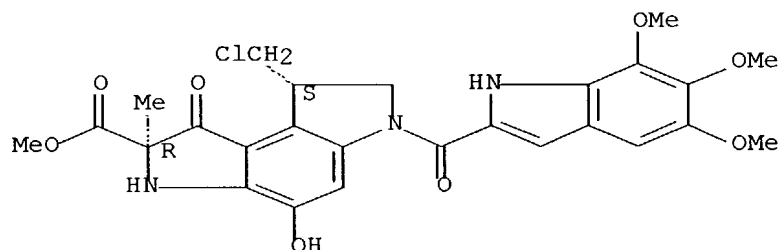
(of *Streptomyces*, structure and antimicrobial and antitumor activity

of)

RN 118292-36-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-4-hydroxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

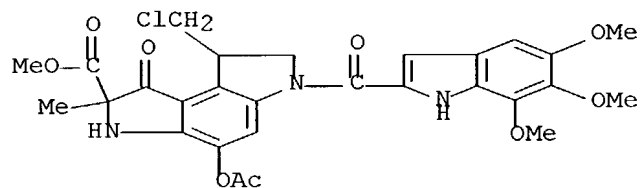


IT **118462-85-4P**

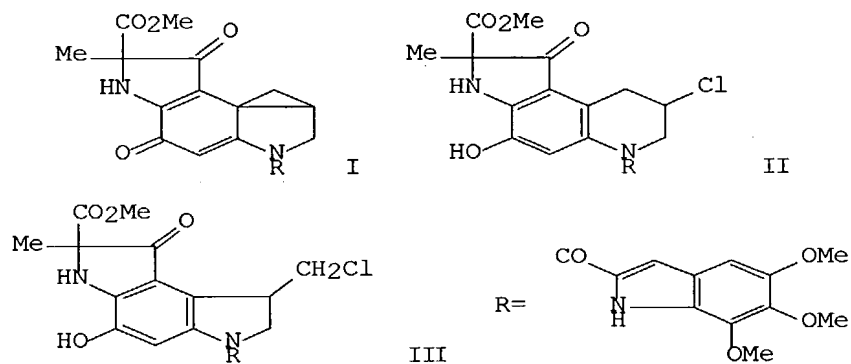
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 118462-85-4 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

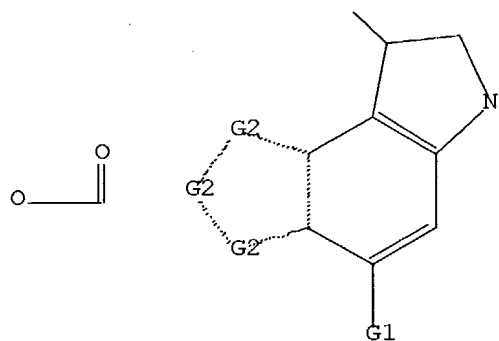


L10 ANSWER 122 OF 122 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1989:38796 CAPLUS Full-text
 DN 110:38796
 TI Structures of duocarmycins, novel antitumor antibiotics produced by
 Streptomyces sp
 AU Yasuzawa, Toru; Iida, Takao; Muroi, Kenichi; Ichimura, Michio;
 Takahashi,
 Keiichi; Sano, Hiroshi
 CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Machida, 194, Japan
 SO Chemical & Pharmaceutical Bulletin (1988), 36(9), 3728-31
 CODEN: CPBTAL; ISSN: 0009-2363
 DT Journal
 LA English
 GI



AB The structures of the new antitumor antibiotics duocarmycins A (I), C1 (II), and C2 (III), isolated from the culture broth of a Streptomyces sp., were determined on the basis of chemical and physicochem. evidence.

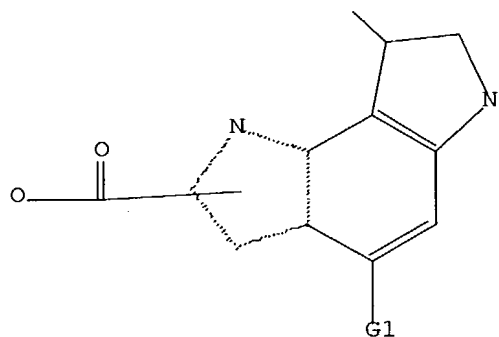
=> d l1; d l5; d l6; d l7; d his; log y
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

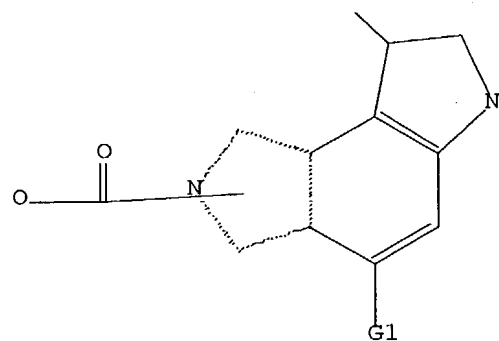
L5 HAS NO ANSWERS
L5 STR



G1 O,S,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

L6 HAS NO ANSWERS
L6 STR

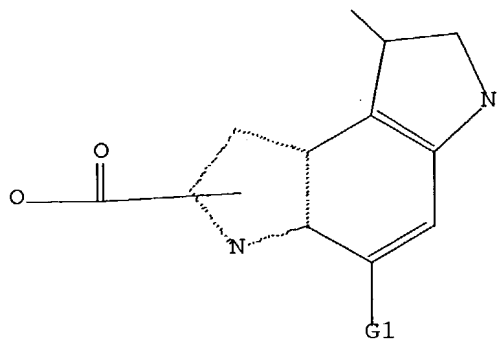


G1 O,S,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

L7 HAS NO ANSWERS

L7 STR



G1 O,S,N

G2 C,N

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 17:58:17 ON 09 APR 2004)

FILE 'REGISTRY' ENTERED AT 17:58:30 ON 09 APR 2004

L1 STRUCTURE UPLOADED
L2 50 S L1
L3 50 S L1
L4 1147 S L1 FUL
L5 STRUCTURE UPLOADED
L6 STRUCTURE UPLOADED
L7 STRUCTURE UPLOADED
L8 50 S L5 OR L6 OR L7 SAM SUB=L4
L9 1001 S L5 OR L6 OR L7 FUL SUB=L4

FILE 'CAPLUS' ENTERED AT 18:05:49 ON 09 APR 2004

L10 122 S L9

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	552.78	749.68
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-84.55	-84.55

STN INTERNATIONAL LOGOFF AT 18:10:23 ON 09 APR 2004